THE CANADIAN MEDICAL ASSOCIATION

# LE JOURNAL DE L'ASSOCIATION MÉDICALE CANADIENNE

JANUARY 7, 1961 • VOL. 84, NO. 1

## FIFTIETH ANNIVERSARY NUMBER

DR. H. E. MACDERMOT
Editor of the *Canadian Medical Association Journal* from 1942 to 1955.

**Dr. H. E. MacDermot's** association with the Journal dates from 1924, when he became a member of the editorial staff under Dr. A. D. Blackader's direction. After serving as assistant editor under both Dr. Blackader and his successor, Dr. A. G. Nicholls, Dr. MacDermot succeeded to the editorial chair in 1942. Assuming responsibility for the Journal at a most difficult time, he successfully directed its publication during the war years and throughout the challenging post-war period. A notable accomplishment during his tenure of office was the changeover to publication twice a month.

Like many other medical journalists, Dr. MacDermot has had a deep interest in medical history. In addition to contributing numerous erudite articles on the history of medicine, he completed the monumental task of recording the history of the Canadian Medical Association from 1867 to 1921, which was published in a scholarly volume in 1935, and he brought the story up to date in a sequel published in 1958.

On the resignation of Dr. S. S. B. Gilder in February 1960, Dr. MacDermot obtained leave of absence from the Montreal General Hospital, where he has served as registrar since relinquishing the editorship of the Journal in June 1955, and returned to the C.M.A. to guide the editorial work until the present editor could assume the appointment.

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### THE FIFTIETH ANNIVERSARY OF THE ASSOCIATION JOURNAL

H. E. MACDERMOT, M.D., F.R.C.P.[C],
*Montreal*

OUR JOURNAL was first issued 50 years ago, in January 1911. Its development since then has paralleled, indeed has been a part of, the growth of the Association of which it is the official organ. It was the first attempt in Canada at a medical journal of definite national scope, although Canadian medical journalism of the day did include publications with a fairly wide distribution. All of these were privately owned and naturally were independent in their editorial policies.

The Canadian Medical Association had been in existence for 44 years before it managed to establish its Journal. A lone voice from England had been heard in 1867, advocating the formation of an official journal, but the newborn Association then and for several years to come was preoccupied with merely keeping alive. Besides, the history of medical journalism in Canada did not encourage new ventures of this kind; there had been several abortive (though praiseworthy) attempts, and very few successes. Dr. R. P. Howard referred to this in his "Report on Canadian Medical Literature of the Past Year" in 1877:[1]

"In a new country like ours," he said, "with a sparse population as yet so youthful that it is composed chiefly of persons whose grandparents were born in other lands, it perhaps cannot be expected that a medical literature should exist.

"Hitherto our professional work has consisted mainly in practising the medical art, and in teaching the science and practice of that art. But few treatises have been written amongst us upon medical subjects, and not one during the past year. It has not yet become a custom among us to write a



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monograph during the early years of professional life with the view to getting patients, nor to edit other men's works with additions not derived from personal experience, but expressing the opinions or experience of others, and let us hope these customs may never become Canadian—still, perhaps more might have been expected from some who have enjoyed large or peculiar opportunities during a long career of public or private practice than they have given to their country in the way of monograph, or treatise, or clinical report."

This criticism was supported by Dr. George Ross of Montreal in another paper on the same subject.[2] He said:

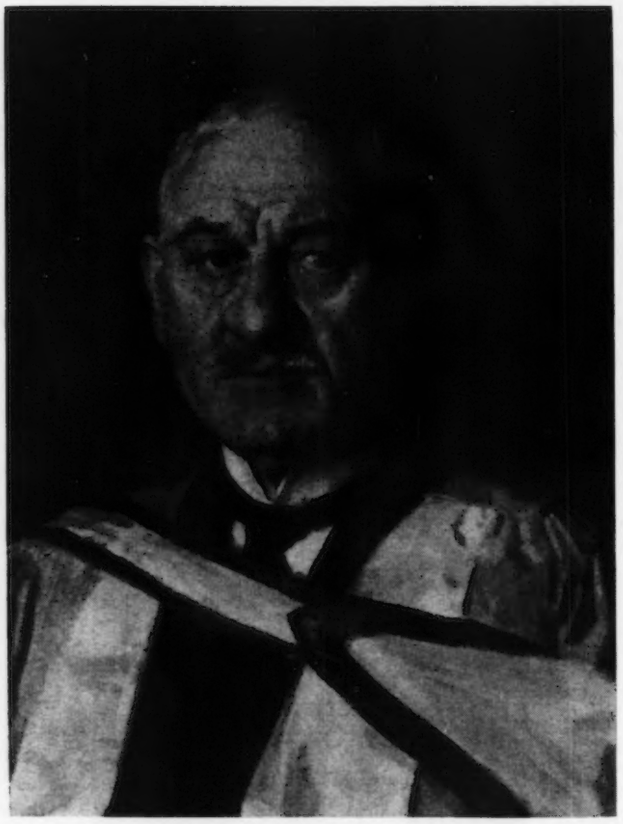
"I am forced to say that, having for the purposes of this paper examined the files of all our native periodicals for the year, I am surprised to find how small an amount of material and how few contributors there are to be found."

In 1907, however, growing activity in organized medicine forced serious consideration of publishing an Association journal. It was clearly recognized that a common medium of expression for the various provincial groups would be of great value in strengthening the Association, whose organization was still very loose.

At first there was strong opposition to the proposal. This came mainly from those who spoke feelingly—and quite accurately—of the difficulty of gaining support for such a journal, and of its great cost. However, the need for closer co-ordination was too urgent to be gainsaid. Probably the most cogent argument was put forward by Dr. (later Sir) Andrew Macphail, who pointed out with his usual precision and forcefulness of expression that existing journals could not afford to publish the Association proceedings and that an Association without some means of recording its transactions and expressing its convictions was largely ineffectual.

Even this might have been no more than good debating, but Macphail went further; he offered to strengthen the hand of the Association by withdrawing from publication the *Montreal Medical Journal*, of which he was then editor. This was a publication with a long and splendid tradition of medical journalism, and to offer its withdrawal was an extraordinary concession on the part of its owners. Macphail had been its editor since 1903, but even before he brought to it his high literary gifts the journal had been outstanding. The only other Canadian medical journal comparable to it was the *Canada Lancet*, published in Toronto, but it had seen its best days (and they had been very good) under Dr. John Fulton (1871-1877), to whose editorship Osler had once paid the following tribute:[3]

". . . Dr. Fulton showed that there was a fine field in Canada for a pushing journal, and he entered in and took possession. His life is a lesson for us all—the lesson that success cometh neither from the east nor from the west, nor yet from the south, but is found in close attention to the everyday details of life, no matter how trivial."



Sir Andrew Macphail
Editor, 1911-1919

With the encouragement from the Montreal group, to which later was added a similar offer of amalgamation from the *Maritime Medical News* of Halifax (1888-1910), the necessary committee work was begun which eventually brought about the establishment of *The Canadian Medical Association Journal*, with Dr. Macphail as editor.

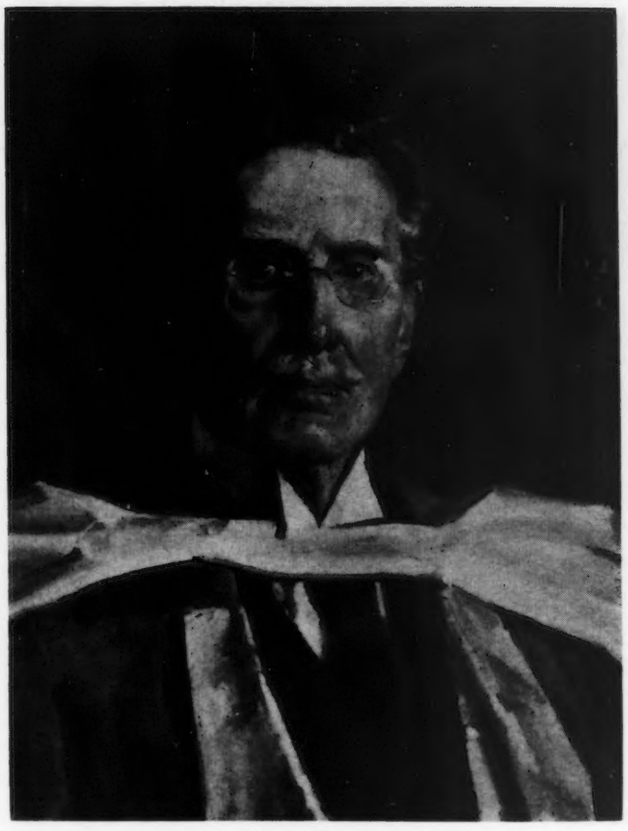
The final notice of the transfer of the Montreal journal read as follows:

". . . The editorial board and the shareholders have arrived at the conclusion that something more elaborate should be attempted, namely, to present Canadian medicine as a coherent whole.

"Accordingly, the profession in Montreal has transferred its journal to the Association, and along with it goes to the larger body a tradition which has existed, and grown, for nearly 70 years. The Association also receives the support of a large and important Medical Faculty, whose sole object is to further the science and art of Medicine for the general good, and not for the advancement of local or individual interests."[4]

Not many journals have come into being so well prepared in advance, but Macphail was under no delusions about his new task. Some time before he had commented on what was involved in keeping up high standards in this kind of journal:

". . . It is, in short, extraordinarily difficult to keep a medical paper on the highest level and at



Dr. A. D. Blackader
Editor, 1919-1930

the same time interest the ordinary reader in general practice. It is between this Scylla and Charybdis that the ship of the Association must be steered. That it is possible to accomplish the voyage, witness the Journal of the American Medical Association; all must depend in the first place upon who is appointed helmsman, and in the second, on the way the crew behaves, or otherwise upon the loyalty and support given to the new Journal by the profession during its early and perilous years."[5]

For the first year at least he carried practically the whole burden of the Journal. An allowance of $125 per month was provided for the editor, but it was understood that this was to supply clerical help; gratuitous editorial work was a tradition accepted without reservation.

Few editors have added to their labours as he did, by voluntarily offering to teach students something of writing and editing. When I was a student at McGill in 1911, Macphail had such a class in the evenings, and as he had already helped me in my first journalistic efforts I gladly went back for more. He would first take a hospital case report and use it to show that even such a lowly form of literature deserved to be carefully written. As a master of prose-writing he spoke with authority, and in his detached, slightly mournful manner he made us comprehend that clearness of expression at least should be within the reach of anyone. Nor was it his fault if we did not realize that this demanded never-ceasing care in the use, and especially the choice, of words. Slang and well-worn clichés drove him to measured malediction. Naturally, he did not try to teach style; he took for granted that each man must develop his own. But he insisted that the importance of what a man was trying to say lay in the style of his expression, not so much in the subject itself. "Take care of the style, and the matter will take care of itself," he would say; which sounded paradoxical, but had more truth in it than was immediately apparent. How apt he would have found T. S. Eliot's lines:*

> The end is where we start from. And every phrase
> And sentence that is right (where every word is at home,
> Taking its place to support the others,
> The word neither diffident nor ostentatious,
> An easy commerce of the old and the new,
> The common word exact without vulgarity,
> The formal word precise but not pedantic,
> The complete consort dancing together)
> Every phrase and every sentence is an end and a beginning.

With the storms of 1914-1918 the Association and its fledgling journal came under almost intolerable stress. Macphail and W. W. Francis, who had become assistant editor in 1912, went overseas on active service,. and with them went also many of the Journal's contributors. The Association held no annual meetings in 1915 and 1916, but somehow the Journal managed to keep going. It is difficult to say who carried on the publication during the war years. The chairman of the Editorial Board, Dr. A. D. Blackader, was probably the driving force, but much of the work was done by Dr. G. G. Campbell and Dr. Maude Abbott, of Montreal. Sir Andrew (as he now was) officially resigned in 1919 (he had received an injury to his eye). Dr. Blackader was virtually editor from then onwards but was not formally appointed until 1923.

The story of the Journal at this time is so closely bound up with the life of the Association that it is difficult to separate the two. The whole organization was in serious difficulties, from which it began to emerge only after the resurgent annual meeting of 1921 in Halifax. One can appreciate something of the growth of the Journal by comparison of its issues year by year. The change from its weakened state to the improved and expanded issues of the mid-twenties depended on several men, but the greatest single factor was the devotion and hard work of Dr. Blackader. At the age of 70 when many think of retirement he made the Journal his sole and all-absorbing occupation, until his resignation in 1930. He had a wide-ranging interest in everything medical and scientific, and unfailing enthusi-

*From "Four Quartets" by T. S. Eliot. Reproduced by kind permission of the publishers, Faber and Faber Limited, London, England.

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asm in teaching. Possessed of a clear style and ability to work incessantly, he had all the essentials of a first-class editor. He always spoke his mind freely and sometimes vehemently, and with his unusually tall, spare figure and dignified bearing, was a striking personality.

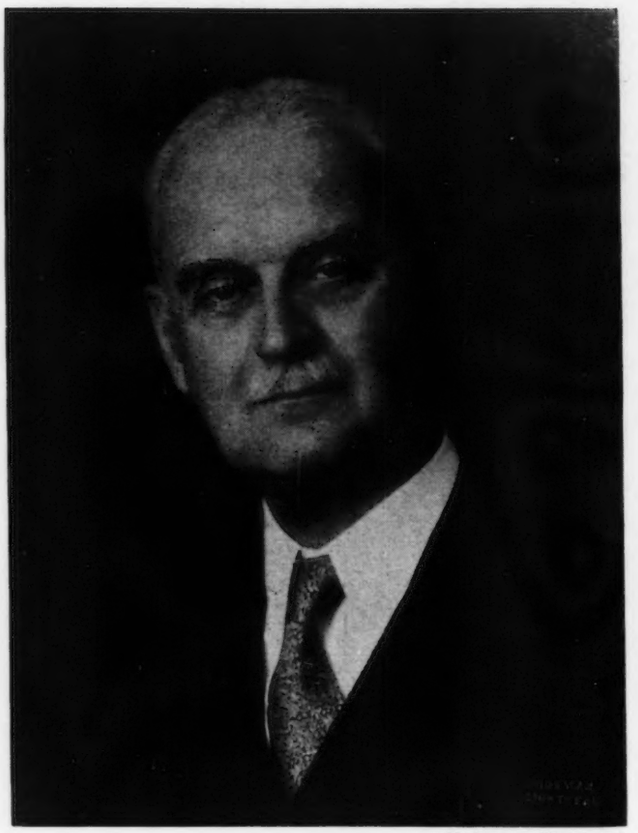
The most urgent task before him was to build up his contributing sources. Much of this he did by direct appeal; he resented it when papers by Canadians were sent to other journals. He would not publish poor material, but somehow he refused few papers. "We must not quench the smoking flax," he would say after looking over a poorly written but not hopeless paper. Not infrequently he would rewrite the article and even add material to it. In my long association with him I would come across instances of such rehabilitation, in which the authors would accept the end product with complacency.

Blackader knew well that the Journal had to earn its place amongst the well-known medical publications, and that he could not offer his contributors a large audience, but he was never daunted. Even during these difficult years he could feel that he was gaining ground. I can well remember the conviction with which he announced at an editorial board meeting in 1928 that now he felt it was time to think of a weekly publication.*

Dr. A. G. Nicholls was editor from 1930 to 1942. He came with a well-earned reputation for careful and steady literary work. The Journal contains much of his editorial writing, always clear and apposite, with touches of humour. As his assistant I have grateful memories of his patience, and he allowed me full opportunity to gain editorial experience. His editorship was in the best traditions of industry and dignity.

My own appointment in 1942 made me realize something of what must have been experienced by the editors during the distractions of the first war, although the comparison did not quite apply, as the Journal now had well-established connections and correspondents, and material was more easily obtainable. The Association meetings continued to be held throughout the war, and the constantly widening activities of the Association, including many connected with the war, provided an abundance of socioeconomic and scientific material.

Increasing attention was given from about 1940 to the inclusion in the Journal of reading matter in French. The feasibility of a bilingual publication had been discussed from time to time, since there were always French-speaking physicians in the Association. However, it had not been found possible to arrange this. Efforts were therefore made to provide résumés in French of selected articles, and these became a regular feature. Naturally, every encouragement was given to our French confrères to contribute papers, and many first-class papers



*Notman, Montreal*

Dr. A. G. Nicholls
Editor, 1930-1942

in English have been received from French authors; there has been a pleasing increase in the number of these in recent years.

It may be added that organized medicine amongst the French members of the profession is represented by L'Association des Médecins de Langue Française du Canada, and that *L'Union Médicale*, whilst not its official organ, has been a highly successful Canadian medical journal since 1872. The relations between the two Associations have been consistently harmonious, and for the present at any rate it is accepted that each body will pursue its own way. A certain proportion of French-speaking physicians will still remain members of both groups; indeed, there is a steady and encouraging increase in the numbers of these in the Quebec Division of the Association. With the conversion of the Journal to a weekly publication the cover design was rearranged to show the title in both languages.

The question of more frequent publication came to the front in 1950. The supply of material seemed to be sufficient to warrant this development, and the advantage of reaching the Association members more rapidly than with the monthly issue was well appreciated. It was only at the beginning of 1955, however, that the Journal began to appear twice a month. The expansion may seem to have been slow in coming, but time was needed to put the Journal on a firm enough footing to justify it. Also, it was not until 1954 that the decision was made

*Actually, this had been suggested as early as 1914, but at neither stage would it have been practicable.

Dr. S. S. B. Gilder
Editor, 1955-1960

to bring the editorial and secretarial offices together under one roof. So far, these had been in Montreal and Toronto respectively, and their centralization contributed greatly to the growth of the Journal. The printer also was now in closer relationship with the editor.

At this time, in view of my impending retirement, Dr. S. S. B. Gilder was appointed editor. Dr. Gilder had been well trained in the *British Medical Journal* office and later had taken up work with the World Health Organization in Geneva. After a few months as co-editor he assumed the full editorship in June 1955, displaying an energy and ability that met the demands of the Journal in its new form with complete success. He carried it up to its expansion into a weekly in January 1960. In February of that year he accepted the offer of another position, and a few months afterwards was succeeded by Dr. Donald Graham of Toronto.

It is difficult in a short review to go into the many details that make up the life of such a curious organism as a medical journal. Those in charge of it naturally are responsible for its well-being, but I have come to think that an important element in its life is the interest taken in it by its readers. The more they feel that they can share in it, the more they will express themselves in its columns by articles or letters or any of the ways which tell an editor that he is getting a response to his labours.

One would expect more frequent use of the correspondence column—that elastic method of expression. But there is a comparative disinclination in our country to write letters; indeed, this seems to be a North American trait, just as an irrepressible tendency to write letters obtains in Britain.

One problem of the day is the gradual alteration in the type of scientific and clinical papers. It is not the literary form of which I am thinking, although that seems to me to be not as good as it was fifty years ago; it is the subject matter which is changing so much. This of course is the result of the steady and rapid splitting of medicine into specialties, making it increasingly difficult for an editor to obtain papers of "general" interest. A paper on even a specialized subject may still be written so as to be of interest to the general reader, but the demand on the author is that much more exacting. Papers on "general" subjects are certainly less frequently submitted. The situation will probably become more difficult; perhaps more symposia and review articles will help to solve the problem.

There is close and important interdependence between the Journal and its advertisers. The complex detail involved in the advertising is dealt with by the advertising department under the managing editor, but final decisions on the advertisements themselves lie with the editorial board. In the early years the necessity for such control became evident when the publishers at the time (Morang & Co.) accepted on their own responsibility some unsuitable advertising. This was corrected, and the editorial and business interests pursue their interlinked existence in unbroken harmony. Our printing has been done since the Journal's beginning in 1911 by the Murray Printing Company of Toronto, from whom we have always had first-class service, under pleasingly friendly relations.

A great deal of steady and to some extent unrecognized work has been done for the Journal by its managing editors; sometimes this office was combined with that of the honorary treasurer. Dr. A. T. Bazin, Dr. F. S. Patch, and Dr. D. S. Lewis held the combined offices for long periods, and steered the business affairs of the Journal through difficult periods. Dr. T. C. Routley was appointed managing editor while still general secretary of the Association, in 1950, and continues his valuable guidance.

The Journal has gradually made for itself the place in Canadian medicine for which the early editors strove so earnestly. If this is to be maintained and the Journal is to be still further built up as a worthy medium for expression of opinion, for recording research, observation and clinical experience, and for keeping the Canadian medical profession informed on the socioeconomic trends which have such a vital bearing on the practice of medicine, there must be continual effort and steady support.

References

1. Transactions of Canadian Medical Association, Tenth Annual Meeting, 1877.
2. *Ibid.*, p. 48.
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4. Editorial: *Montreal M. J.*, 39: 818, 1910.
5. Editorial: *Ibid.*, 38: 680, 1909.

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# FIFTY YEARS OF MEDICINE: 1911-1961

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IN THE five decades which have elapsed since the founding of the Journal man has travelled far and dangerously, and the record of his pilgrimage is bewildering in its complexity and challenging in its extent. No period since the Renaissance has seen such cosmic drama, upheaval of thought, or social change. Within this short span the entire face of the world and the character of human thought and belief have been wholly transformed.

No area of human life better exhibits this revolutionary change of outlook, this increasing tempo and this creative genius for good or evil than medicine. The history of medicine has always been in large part the history of life and civilization. It embraces all the sciences, and yet remains an art. It reflects all the foibles and glories of mankind. It unites tradition and invention, and, while adopting the jargon of modern science, it continues with its ancient humanistic piety to address life and its ailments in polite, if not always accurate, Latin and Greek.

The extraordinary advances of medicine in this century keep the mind constantly alert, and it is difficult to strike a proper balance of language when indicating their extent and influence. Trying to bring the whole into proper perspective, the medical historian must engage Time as an ally if he is to escape a too presumptuous or too belittling attitude to the present and to eternity. In all humility he will remember von Ranke's dictum that each moment of time and history is equidistant from eternity, thus dismissing the popular shibboleths prating of progress. And finally, there will be in his mind the words of Claude Bernard, the finest expression of the medical view of progress, that science increases our power for good only in proportion as it lowers our pride.

The word "progress", inescapable in a discussion of this sort, itself has an ironical ring. It is a sobering fact that most of those who survey the march of history during the past fifty years end on a note of dark misgiving and almost fatalistic despair. Under the impact of two world wars and the ominous possibility of a third, a belief in progress has become a dim and dated illusion. Nevertheless, to even the most gloomy pessimist the advances of medicine offer hope and consolation. For the fact of progress is written plain and large on the pages of medical history. Here, in the logic of discovery, the development of ideas, and the application of knowledge to human needs, lies the vitalizing and redeeming spark of human history.

Despite its shortcomings, medicine stands today as one of the great triumphs of the human spirit. Through the past century of turmoil and war, it has continued to engage knowledge in the struggle against disease, and in that task has recognized no natural boundaries and known no enemies. As a result we are confronted by the ironical paradox that at a time when man has been scourged by fear as never before, he has never been so safe against the threat of disease. This is not the expression of easy optimism or self-satisfaction. It is possible to take pride in the progress of medicine and at the same time remain humble and chastened in the face of the virtues of the past and the follies of the present.

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So much has happened in medicine in the past fifty years that any assessment of the range and significance of the many events is exceedingly difficult. Our notes of necessity must be highly selective. But such an exercise may serve to stretch our minds a bit. The historical memory of the majority of people even in a reasonably well educated democracy has a backward stretch of about five years. What lies in time before that is thought of as the good or bad old days, legend or vague history, a few names and dates in misty perspective. To most Canadians even "Passchendaele" is little more than a word now.

In addition to that, a backward glance at the medicine of this century is a liberating experience. We see medicine under the impetus of science and and social reform bursting old bonds of custom and dogma, expanding on a myriad of fronts, and reaching its present stature. These same developments have been reflected in Canadian medicine. In a word, we are today living in what might properly be described as the medical renaissance.

In this celebration of a half century of medicine we are asked to deal with that part pertaining to medicine — that is, that field of practice which excludes surgery, obstetrics, gynecology and a small legion of other lusty divisions. And here is where the charming inconsistencies of medical custom and usage, so exasperating to the layman, begin to appear. For how in the name of all the medical gods are we to define "medicine"? It is surely hydra-headed with appendages bearing all sorts of strange names — cardiology, endocrinology and the like — and includes that triumph of enigmatical nomenclature — internal medicine. Even Osler gives up the task of definition, and, with a bow in the direction of his own field of work, dismisses "medicine" as that group of practitioners which "bears without reproach the good old name 'physician'". In any event, medical men somehow know the distinction, and we may let it go at that. At the same time, looking particularly at the colossus of surgery, we will be at pains to preserve the niceties of medical etiquette, exercising all the while a degree of tolerance and charity. But we may add that under the eye of eternity, to all who live by the practice of medicine — physicians and surgeons alike — the master question in consulting room, at the bedside and at the postmortem table

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*Former Chancellor of the University of Alberta.

remains, "What, in the name of Hippocrates, is the matter?", the question so eloquently visualized in the picture by Luke Fildes which shows in paint rather than sculpture, in the manner of the later Rodin, an absorbed middle-aged man, the Medical Thinker, stroking his beard and wondering just what is the matter with the sick child on the bed before him.

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1911-1961. Two generations. To illuminate the story of medicine it must be seen in the matrix of society, within the web of its relationships with science, social reform, industry, government and religion. Let us glance at the years of grace 1910-1911. The Edwardian age came to a close with the death of Edward VII. Woman suffrage was the lively topic of the day. Theodore Roosevelt was acting as an equally lively catalyst on the American scene. The automobile was beginning to be accepted by the horse. The two popular songs of the time were harbingers of a new order in technology and art — "Come, Josephine, in my Flying Machine" and "Alexander's Ragtime Band". The Gibson Girl drawings were the pin-ups of the day. In Canada the Laurier government was in the midst of the great reciprocity debate. The perennial themes of the school question and the high cost of living were being discussed as hotly as ever. Ralph Connor's books were the popular reading. Medical delegates to the Canadian Medical Association meeting in Edmonton paid $59.00 for the round trip from Montreal. The population of Canada in 1911 was listed as 7,204,772.

The feeling of youth was still in the air. Alexander McPhedran in a presidential address to the Canadian Medical Association spoke of "Canada, in these her yet salad and hoydenish days"! And Andrew Macphail in an editorial in one of the first numbers of the Journal (1911) wrote: "A Canadian type of nationality and a Canadian type of disease are in process of formation, and Canadian physicians are quietly and surely laying the foundations for a Canadian medicine of the future." In the phrase of the time, the twentieth century belonged to Canada.

In this climate medicine was still, broadly speaking, a single, almost comprehensible whole. The general practitioner was still the dominant factor, in training and in practice. Specialization had not yet cut any notable divisions. There was much therapeutic nihilism. Therapy was aimed at symptoms, did not remove causes. The *vis medicatrix naturae*, the great balancing agent in disease, was doing a yeoman job. Indeed in the decade 1910-1920, as someone has said, for the first time in history a patient going to a doctor had better odds than 50:50 of profiting by his visit.

The medical scene was stable enough. Techniques of physical examination and clinical discipline were foremost (but there were no "physical check-ups" and mental disorders were still "insanity"). Then came morbid anatomy, bacteriology and a simple clinical pathology (lumbar puncture was just coming in). Therapeutics was the weak field. A cynical teacher used to tell us that the only disorder we could hope to cure was the itch, and then, in more optimistic vein, added that if we mastered the use of morphine and digitalis, therapeutics-wise all else would be added unto us.

The chief concern of the profession was infectious disease, notably the ravages of typhoid fever, tuberculosis and syphilis ("606" was beginning to be widely used). By the same token, questions of public health — guarding of water supplies, pasteurization of milk, sanatoria — were much in the air. The x-ray was in its early adolescence. Great concern was being felt at the high infant mortality rate and the ravages of epidemic disease. On the organization side the historic Flexner Report (1910) on medical education spurred great changes in undergraduate training, and presently medical schools passed under the complete control of the universities. Re-reading this report today is almost like reading about the dark ages. After long and bitter controversy the requirements for licence to practise and a measure of central control of registration were formulated and the Dominion Medical Council came into being under the terms of the Roddick Bill (1911). This together with the establishment of the Journal under the editorship of a man who was to become a great figure in the literary life of Canada, Sir Andrew Macphail, served to cement more solidly the widely scattered profession from the Maritimes to "the North-West". In reading over the old files dealing with these matters it is interesting to note one item prophetic of things to come. In the February 1912 issue of the Journal, the Editor, in a tone of sarcasm and sorrow (a blend that Macphail could command), commenting on a recent wildly irresponsible "Medical Profession Act" passed by the Province of Alberta, remarks: "Alberta is again proving itself to be a *most valuable laboratory for experiments in legislation*, and with the courage of youth it does not count the 'cost' of the service which it is rendering." (The italics have been added.)

But all the while a new and revolutionary era for the world and medicine was just over the horizon. 1914 was approaching. The end of the old order of medicine is well symbolized in the funeral of Lister in 1912, so eloquently described in the pages of the Journal by Sir William Osler in the section "Men and Books" (*Canad. M. A. J.*, 2: 343, 1912): "I have just come from the Abbey service—the most splendid tribute ever paid to our profession, and so richly deserved in the person of Joseph Lister, one of the greatest benefactors of humanity."

The dawn of the twentieth century had found medicine firmly established on the scientific side upon physiological investigation, and advancing rapidly with new concepts and tools. This increasing body of knowledge derived from the special

sciences rapidly brought into being new divisions of medical work, thereafter expanding on many fronts. From 1910 on, medicine was rising to a crest under the influence of a host of new discoveries and disciplines. The fruits of the bacteriological era were reaped in the control of infectious disease, freeing man from the scourge of epidemics and making possible the southward march of civilization into the tropics. On every sector of medicine the boundaries were pushed forward rapidly – public health, hospitals, nursing, laboratory, diagnosis, nutrition and, above all, therapeutics. Under the stimulus of these achievements medicine entered the period of scientific subdivision and, aided by the many social reforms of the time, achieved its present stature and position in the world.

This medical drama was enacted against the backdrop of a catastrophic world scene: the few golden years before August 1914 . . . August 4, 1914, when the lights of Europe started going out one by one . . . the war of 1914-1918 . . . the "gay twenties" . . . the great depression of 1930 . . . the thirties, more serious, apprehensive of war and yet aware of being carried towards it . . . Communists and Fascists battling to the destruction of civilized values, with the sinister figure of Hitler darkening the sky . . . the war of 1939 . . . the atomic bomb in 1945 . . . the exasperating years since 1945. What folly, evil, despair and strange glory are contained in this cavalcade of years! In the perspective of history the only time that seems to parallel it is the interval from the conversion of Constantine to the sack of Rome.

* * * *

Turning more directly to the actual advances in medicine during the period under review, we can begin with something in the nature of a summary estimate. It has often been said – and with truth – that during the past fifty years medicine has made more progress than in all the previous centuries of the life of man upon the earth. This came on the heels of the achievements of the nineteenth-century, what Osler called the Promethean gift of that century to man – "the great boon – when the leaves of the tree of science have been for the healing of the nations". To paraphrase Tennyson one could say: "Better fifty years of modern medicine than a cycle of Cathay." In this respect medicine has reflected the currents of the age which in its fund of knowledge, as well as its material endowment, has been transformed to a degree probably without equal in history. As Oppenheimer said recently, so rapid has been the advance of knowledge that 90% of all knowledge possessed in the world today has been discovered since we of the older generation were in school.

Some of the more important medical discoveries, events and trends may be indicated in a tabular way, to give point and substance to these glittering generalities. In most cases these are not the outcome of the work or genius of one man or one group or one nation. Each discoverer has built on the foundations laid by his predecessors:

Ehrlich's discovery of salvarsan (1910) which laid the foundation of what has since been termed "chemotherapy".

Hopkins's demonstration of the vitamins (1912), giving the key to deficiency diseases and launching the science of nutrition.

Developments in the physiology of the nervous system, notably the monumental contributions of Sherrington.

Three dynamic movements in psychology and psychiatry, connected with the names of Kohler, Pavlov and Freud. The ideas of Freud and his successors changed a pedestrian branch of medicine into a vital science of the mind of man which has penetrated every nook and cranny of our social fabric and has had a profound influence on philosophy and on the arts–music, visual art and, notably, literature – and has brought about a revolution in the sexual mores of our time.

Synthesis of drugs, beginning with veronal in 1903.

The isolation of thyroxin by Kendall (1917), reflecting an increasing knowledge of the hormones.

Banting and Best's discovery of insulin (1922). Collip's discovery of parathormone (1925).

Minot and Murphy's application of Whipple's previous observations in the introduction of liver for the treatment of pernicious anemia (1926), leading to the isolation of vitamin $B_{12}$.

Domagk's discovery of sulfonamide (1935), initiating the age of antibiotics.

The introduction of penicillin by Fleming, Florey and Chain (1941).

Vaccine and antitoxin therapy in a wide range of lethal diseases, notably Salk's poliomyelitis vaccine (1953).

The discovery of the effects of cortisone and ACTH by Hench, Kendall and Reichstein (1948), which started a chain reaction of further biochemical studies.

The observation that DDT could control the mosquito as a vector in disease, followed by the advent of more potent antimalarial drugs, chloroquine and primaquine, since 1945.

And in a more general way:

The increasing development of diagnostic and therapeutic x-ray measures.

Widening concepts of cardiovascular disease and the development of anticoagulant drugs.

The growing influence of so-called psychosomatic medicine permeating and quickening the whole of medical practice.

The growth of public health and industrial medicine.

The increasing importance of geriatrics, bringing a new dimension into medicine.

Physical medicine, rehabilitation and new ideas with regard to convalescence, enlarging the horizons of practice.

For medicine the results of these and a host of other achievements taking place in such a short space of time have been profound. Some of these results are the end of the physician as an individualist, the growth of specialism, the increasing claims of what has come to be called "social medicine", an uneasy impersonalization of medical practice. For society the results have been equally far-reaching. Life expectancy in 1910 was 52 years; today it is in excess of 70 years. In 1910 pneumonia (and influenza) and tuberculosis were the most common causes of death. In 1960 they are the least common of the seven leading causes of death, heart disease and malignancy (diseases of older people) heading the list. The mortality in infancy and childhood has declined by 80%. Chronic disease is now a major problem. In short, the thing called living, in both medical and social terms, has had almost literally to be learned all over again.

It should be noted that during these decades medicine suffered one of the most painful chapters in its history when Nazi doctors used Jews and many others for experiments, and connived in mass murder and mass slaughter. Physicians with mankind at large witnessed the monstrous insult to human life and dignity in the use of the atomic bomb, a reversion to the savage destruction of societies practised by Attila and the barbarians.

* * * *

In a rapid survey such as this one must pause for reflection. Certain things are evident. For one, medicine is too close to man ever to become absolute, but, though subject to fad and error, is constantly corrected by its contact with the immediate and the basic imperatives of life and death. This sharing in the universal plight of the individual man breeds the moral component which is in the very fibre of medicine and those who practise in its ranks. And in turn medicine must always be important to a people because it is bound up with their fate.

There is the further reflection that in medicine the power conferred by science but linked with a liberal tradition of wisdom, a regard for life and human values, and a concern for social reform can bring a new and brighter world for man, a liberation from disease, misery, ignorance, superstition and fear. It can give man a new assurance and faith in his destiny.

Medicine is part of its time. As Whitehead has said, for physicians it is no longer "a field in which sheep may safely graze". In our modern age it has been profoundly affected by four gospels — those of Darwin, Marx, Freud and Einstein. But in the welter of opinion it has gone its own way and, except in a few instances, has been singularly free of *debunking*, that solace for idiots who do not want to take the trouble to understand or appreciate. In its course it has been profoundly affected by the influence of the spirit of William Osler, who continues to cast his beneficent and humanizing shadow over modern medicine in all lands. This medical prophet, "born", as a recent American writer has it, "in the wilds of Upper Canada" (practically the Toronto suburbs no less), still speaks in the accents of the great tradition, stimulating scholarship and research, counselling idealism as the cornerstone of the profession, and reminding us of medical practice as a high adventure and of medicine as an art.

* * * *

Medicine in Canada has reflected the developments which have been outlined above. The main influence, at first British and European, gradually became American, as the principal shrine of medical thought and teaching has shifted from one centre to another. Three medical schools have been founded since 1910 — the Medical Faculties of the University of Alberta in 1913, the University of Saskatchewan in 1926 and the University of British Columbia in 1950. The Canadian Medical Association was reorganized in 1921 with Dr. T. C. Routley as its first full-time secretary and has steadily grown to its present stature. Medical research with, in the early years, few laboratories and only a few qualified workers, at first (1916) under the direction of an Honorary Advisory Council (with Dr. A. B. Macallum the first chairman) and later the Medical Division of the National Research Council, has substantial achievements to its credit and has given Canada a place in the medical world.

Something of the record may be indicated in a very cursory and inadequate way:

The world-acclaimed accomplishments of Banting and Best in the discovery of insulin (1922) and of Collip in the isolation of parathormone (1925) have already been referred to.

Bruce Robertson introduced the technique of transfusion by the use of multiple syringes (1913) and later (1921) performed the first exsanguination-transfusion in children with severe burns.

W. E. Gallie established the value of living sutures in surgery (1920).

The Connaught Laboratories under J. G. FitzGerald (1924) started work on toxoid and antitoxins, later developing zinc insulin (D. A. Scott) and the large-scale production of heparin (Best, Scott and Charles).

Henderson, Lucas and Brown developed the anesthetic, cyclopropane (1928).

Collip at McGill University separated and identified the hormone of the anterior pituitary gland (1933).

Norman Bethune of Montreal set up the first practical blood bank during the Spanish Civil War (1934).

Gordon Murray, with the use of heparin, performed the first successful grafts of blood vessels (1935).

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Burton, Hillier and Prebus produced the first successful electron microscope on this continent.

The work of Selye on the reactions of the organism to injury has given rise to the concepts of the alarm reaction and the general adaptation syndrome which have influenced medical thought all over the world.

Maude Abbott's classical work on congenital heart disease helped to lay the foundations of modern cardiac surgery.

Wilder Penfield made his monumental contributions to the physiology of the brain (1930 on).

H. E. Johns, working at the University of Saskatchewan, constructed the first cobalt-60 beam therapy unit in the world (1951).

Speaking more generally, mention should be made of the work in various fields of the Banting Research Foundation, the contributions of the Montreal Neurological Institute to our knowledge of disorders of the nervous system, the many activities of the Hospital for Sick Children, Toronto (notably the work of F. F. Tisdall on nutrition), and other contributions from various centres across the Dominion. All have added to the rising tide of Canadian medicine. The main agencies of development are now the university faculties of medicine, the large hospitals, and the great company of men trained in clinical and laboratory investigation and in internal medicine throughout the nation. Under the modern dispensation medical progress in Canada as elsewhere involves teamwork and is the result of the labours of countless men and women. Further developments will be aided by the increasing provision of postgraduate training in Canada, an end towards which W. E. Gallie and the McLaughlin Foundation have already contributed in such an effective and imaginative way.

* * * *

In thus looking back at the changing medical scene over the past fifty years we have been exercising posterity's small prerogative of irony. The outlines have been sketched roughly and inadequately, but the scribe may take some consolation from the words of old master Thomas Fuller who wrote: "There is no danger in meddling with history, which is a velvet study and a re-creation work." What has been set down, however, has been written in the spirit of the noble Roman virtue of *pietas* – respect before the figures and the memories of the past, a salute to past endeavour in the face of time and the elements, a firm belief that the dust of the past is always organic.

What these physicians of the past fifty years – many of them heroes of the writer's medical youth –thought of it all we can only conjecture. But the record makes it plain that they worked under the compulsion of the great verities of medicine, and that their trials and assumptions and judgments were in the main ours. It is in this realization that we can see the firm continuity of medicine, something in which each generation of physicians has a life interest, something received with the acknowledged duty of improvement, and transmitted with the duty discharged, as much as lies within human power. Under this discipline there are few other searching or ultimate questions to be asked – and in any event, there are no final answers in medicine.

The medical pilgrimage that we have been considering was undertaken and completed under the arc of a wide necessity and lit by horizons that change and never end. The legacy is ours as medical men and Canadians.

> "For the deeds of the past are, indeed, an inheritance common to us all; but the ability to make proper use of them . . . is . . . the gift of the wise" (Isocrates, *Panegyrics*, 9).

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## QUEEN'S AND THE CARNEGIE REPORT

(Editorial, reprinted from the *Canadian Medical Association Journal*, 1: 62, 1911)

In Publication No. 2, December 1910, issued by the medical faculty of Queen's University, the Carnegie report on medical schools receives trenchant criticism. The faculty considers that the report has been proved to be frequently inaccurate in its statements of conditions, and that, if the inspection of other schools was made in as superficial and rapid a manner as, it claims, was the case at Queen's, many incorrect statements must have been made and many impressions received not justified by facts.

Although piqued, the faculty believes that it is justified, in view of the hurried inspection, in not taking the report very seriously. The inspection of Queen's by Mr. Flexner and Dr. Colwell occupied part of an afternoon. The registrar of the university gave these gentlemen some general information, and it was only by chance that the dean accompanied them through the General Hospital and the medical buildings. In the evening Mr. Flexner and Dr. Colwell were entertained at the club, and it was after midnight when they left Kingston. It was this untimely departure, the faculty thinks, rather than the earlier dinner, which gave them such a gloomy impression of the future of Queen's medical faculty.

The passages in the report to which objection is taken are those which criticise the clinical opportunities of the school,—"the clinical facilities are limited"; "obstetrical cases are too few"; "the opportunities for out-patient work are slight"; "the clinical years require much more [material] than the town now affords." These statements are considered as fairly reasonable but as not representing the exact conditions. In their report, Mr. Flexner and Dr. Colwell set down the average number of beds as eighty, these being in the Kingston General Hospital. Upon these beds, the report states, the school relies mainly. The faculty points out that in the General Hospital there are over one hundred and fifty beds, with practically all the patients available for clinical purposes; in the Hôtel Dieu, about the same number, at least one-half of whom may be used for teaching purposes; and at the Rockwood Hospital over five hundred patients, all of whom are available for clinics. As for obstetrical cases, the faculty notes that the report does not show that there is any school where the obstetrical cases are considered sufficient in number, and claims that Queen's students have as many as those of other schools.

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# FIFTY YEARS OF SURGERY: 1911-1961

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IN THE FIELD of surgery, the fifty years which have elapsed since the *Canadian Medical Association Journal* issued its first number have been marked by great technical advances and major contributions to knowledge. To have lived in this period has been an exhilarating experience. I speak as one who has been granted such experience, for I entered medicine in 1910 and my medical career therefore coincides with the fifty years of publication of the *Canadian Medical Association Journal*. This probably has been the greatest period in the history of surgery, exceeding in its accomplishments even the revolutionary changes which followed Lister's discovery of antisepsis. Lister's work, it is true, contributed largely to a solution of the problem of "hospital diseases", and thereby made possible an entirely new approach to surgical problems. The far-reaching effects of this came to fruition in the first half of this century and the harvest of new techniques and new knowledge has been rich and enormous. When we review this period, it is with pride that we remember that many of the advances were contributed by Canadians. It is therefore particularly appropriate that the *Canadian Medical Association Journal* should place on record what has been accomplished in surgery in the fifty years of its publication.

Wars have always exerted a profound influence upon the course of surgery, and many new surgical developments derive from war experience. This has been conspicuously true in the last fifty years, for the two great wars which occurred in that period profoundly influenced surgical thought and practice. Because of this it is convenient to divide the era into periods interrupted by the two wars: The Prewar Period, 1911-1914; The 1914-1918 War; The Period between the Wars, 1918-1939; The 1939-1945 War; The Postwar Period, 1946-1961.

## THE PREWAR PERIOD — 1911 TO 1914

In 1911, when the *Canadian Medical Association Journal* commenced publication, surgery was still expanding under the emancipation from complications and mortality which derived from Lister's introduction of the antiseptic principle. By then, aseptic surgery had supplanted antiseptic surgery, and by emphasizing the need for scrupulous cleanliness in the operating room had transformed hospitals into temples of Hygeia rather than the cesspools of filth of pre-Listerian days. The success of asepsis in eliminating infections made it possible to operate upon any part of the body accessible to the surgeon's skill, unhampered by the dreadful "hospital diseases" which brought death to such a high proportion of those patients operated upon before Lister's discovery. Perhaps it is an overstatement to imply that infection was eliminated. There always existed the possibility that the aseptic ritual might be faulty and permit the operative field to be contaminated. Moreover, the risks of airborne infection were not understood and masks were not worn. Nevertheless, the gross catastrophes which were commonplace in the pre-Listerian era were prevented; operations could be performed with reasonable certainty that the patient would escape death from infection and that the wound would heal. When infection occurred, as it did from time to time, it was a misfortune. Certainly the more meticulous the adherence to aseptic principles, the greater was the freedom from operative complications.

Freed from the bane of postoperative infection and its attendant mortality, surgery was vigorously developing perfection of techniques which would permit the exposure and removal of diseased tissue in every part of the body for the first time in history. This was a challenge, and each year brought advances which permitted new areas of the body to be exposed and old problems hitherto incapable of cure to be brought under control by surgical extirpation or repair. It was an era which invited ever increasing skill and refinement of technique. It produced a generation of master craftsmen whose courage and skill enabled them to conquer old problems by new methods.

It would be wrong, however, to imply that the surgeons of that day were merely superb technicians. On the contrary, the technical skill with which they exploited opportunities afforded by the safety of aseptic surgery enabled them to see disease as well as to remove it. They learned the pathology of disease before it reached the end stage revealed in the postmortem room. They founded the science of surgical pathology (pathology of the living) and clarified the nature of many disorders hitherto obscure, such as perityphlitis (appendicitis), empyema, congenital pyloric stenosis and peptic ulcer. This was a time when surgeons were more expert in the diagnosis of certain diseases than were physicians, and more knowledgeable of pathology than were pathologists. They made full use of their opportunities, and many of the best textbooks of the day were contributed by surgeons who spoke with authority on the diagnosis and pathology, as well as on the treatment, of such conditions as cholecystitis (Moynihan) and diseases of the breast (Cullen).

One conspicuous example of this new type of surgeon was Harvey Cushing, whose career as a neurosurgeon was established in 1908 when he wrote the section on surgery of the head in Keen's *System of Surgery*. From that time almost until his death in 1939 he was the world's leading neurosurgeon. Much of its art was his own creation and as the years passed his work was continued by the men he had taught. His pupil, Kenneth McKenzie of Toronto, established this specialty in Canada in 1925 and created a Canadian school of neurosurgery. Wilder Penfield, though not a pupil

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of Cushing, was much influenced by his work and adopted the special techniques which Cushing developed to make neurosurgery possible. In 1944, a happy combination of circumstances (the vision of Edward Archibald, a generous grant from the Rockefeller Foundation and the availability of the right scientist-surgeon) led to the establishment of the Montreal Neurological Institute with Wilder Penfield as Director. It was the first such institute in the world. Its work has brought fame to Canada and the Order of Merit to its Director.

Cushing was compelled to develop meticulous new techniques which made operations upon the fragile tissues of the brain and spinal cord possible and safe. Equally important were his contributions to the physiology and pathology of the central nervous system derived from the observations made during operations. By the correlation of history, clinical picture, operative findings and the histology of the lesion derived from his careful records, he acquired more knowledge of the physiology and pathology of the central nervous system than that possessed by the neurologists of his day. In 1923, in his presidential address to the American Neurological Society he gently commented, "That surgeons should be admitted into this intimate guild now nearing its half century of existence speaks well for the open-mindedness of its members. And if any of you have misgivings as to our acceptibility here, on the basis that metaphysicians and artisans make an impossible social mixture, we can only hope that time will justify your action by our becoming better neurologists and your becoming more familiar with handicraft as a therapeutic measure for certain maladies." Cushing delivered the Balfour Lecture in Toronto, in 1931, on "The Relationship Between the Diencephalon and Gastric Ulcer". On this occasion he presented the first evidence that cerebral impulses could so modify the vagal influence on the stomach as to produce peptic ulcers. It was a revolutionary concept that has been supported by subsequent clinical observations.

By 1911 a new field of surgery was emerging: the transplantation of tissues. It was a new thought that benefit might be obtained from the transference of tissues from one part of the body to another, or even, at times, from one person to another. There had been earlier pioneers in this field. Hunter long ago had successfully transplanted teeth in human beings, and cocks' spurs to cocks' combs. Alexis Carrel had attempted the transplantation of organs. These experiments, however, were philosophical in nature, intended to throw some light on the nature of living organisms rather than to develop measures for the therapy of disease. Of more immediate and practical value were the contributions of Ollier (1872) and Thiersch (1874) in the field of skin-grafting. But these were men in advance of their time. In Canada at least, it was not until the war of 1914-1918 that great need for skin grafting arose, and not until then was the merit of Thiersch grafts really appreciated.

In 1912, Macewen of Glasgow published his monograph on "The Growth of Bone", which included a section on the transplantation of bone. In 1913, Hibbs, and Albee, independently and within a few weeks of each other, published papers on the treatment of Pott's disease by spinal fusion. This initiated a productive period in orthopedic surgery in which the merit of bone grafting in the treatment of a great variety of orthopedic problems was extensively explored. From these investigations many valuable new procedures have evolved. Enquiry into the principles underlying bone grafting still dominates orthopedic research, for the success which Macewen, Hibbs and Albee achieved by their empirical approach raised fundamental problems, many of which still remain to be solved.

Amongst those who played a leading part in the new field of transplantation of bone were W. E. Gallie and D. E. Robertson of Toronto, whose studies have become classics. These led in turn to research into the transplantation of fibrous tissues, particularly of fascia lata, by W. E. Gallie and A. B. LeMesurier, and the application of this form of tissue transplantation to the repair, by living sutures, of such surgical problems as hernia, recurring dislocation of the shoulder and recurring dislocation of the patella.

The transfusion of blood may well be included among these ventures in the transplantation of tissues. Over the years many crude attempts were made to transfer blood from one patient to another. Crile's procedure (uniting an artery of the donor to a vein of the recipient by means of a cannula) was the first successful method of direct transfusion, but it had many shortcomings, chief among which was the impossibility of knowing the exact amount of blood transfused. I believe that Alexander Primrose was the first to use this method in Toronto, and his case books record two or three spectacular successes as well as his enthusiasm for this new therapeutic measure. Lindeman's multiple-syringe method provided the first practical technique for direct transfusion. It avoided the problem of blood clotting by transferring the blood quickly in small amounts by 20-c.c. syringes. The quantity transferred could thus be precisely measured. Bruce Robertson learned this method in New York and introduced it to Toronto late in 1913. When Bruce Robertson went to war with No. 2 Canadian Casualty Clearing Station, he adopted this method in the treatment of patients with war wounds with gratifying success, as he reported in the *British Medical Journal* in 1916. This perhaps is the earliest documented report on the application of blood transfusion in the treatment of war wounds. When we remember that the importance of blood groups was not then fully appreciated, it was a bold and imaginative decision on his part to transfuse soldiers exsanguinated by wounds. A few of his patients developed hematuria and one

died, after multiple transfusions, perhaps from a transfusion reaction, but many were saved by blood replacement. In Toronto, Lindeman's method continued to be used for many years after the 1914-1918 war before it was finally replaced by transfusion of citrated blood.

From 1910 to the beginning of the 1914-1918 war, the surgical world of Canada centred about personalities. Mr. Cameron, the cultured and urbane professor of surgery in Toronto, was still devoted to the early principles of aseptic surgery. He never wore gloves but he finished his handscrub with mustard. George Bingham, A. Primrose, Walter McKeown, H. A. Bruce, C. B. Shuttleworth, George Peters and F. N. G. Starr were all dynamic individualists whose skill and technique won them separate personal followings. A similar situation existed in McGill. But there was a ferment of new ideas in the air. For the student of that day, medical literature was filled with fascinating reports of new work. The merit of the new drug, salvarsan, devised by Ehrlich in his 606th experiment to find the "silver bullet" which would constitute a specific chemical formula for the cure of syphilis, was under assessment. The intricate mystery of the antigen-antibody reaction was being unravelled. The earliest electrocardiograph was installed in the Toronto General Hospital in 1913. It was an Einthoven string galvanometer which occupied an entire room in the basement of the new hospital on College Street. The beam from its mirror was projected on to the opposite wall of the room and there recorded its feeble oscillations upon a strip of sensitized paper. Dr. John T. Fotheringham still arrived with dignity at the College Street entrance in his dogcart with coachman, but Clarence L. Starr snorted about in a fabulous new mechanical wonder, a White Steamer. This period of picturesque individualism ended with the first war. With the restoration of peace, the appointment of C. L. Starr as the first full-time professor of surgery initiated a new era in which the staff became a team working towards the advancement of surgery as well as the teaching of students, the treatment of patients and the nurture of private practice.

## THE 1914-1918 WAR

When the 1914-1918 war erupted, surgical knowledge was ill-prepared to deal with its problems. As far as the British Empire was concerned, there had been no experience in war surgery since the Napoleonic wars, save for that gleaned in the Crimean and South African wars. For America, the last experience in war surgery was that of the Civil War. The first and last of these conflicts preceded the antiseptic era, and the medical problems of the South African war were centred more on illness than on wounds. In the latter conflict far more soldiers died of typhoid fever than of shot and shell. For two generations surgeons had disciplined themselves in the principles of aseptic surgery. It was difficult for them to appreciate that the shattering wounds and compound fractures produced by shell fire were grossly contaminated with bacteria and that the tissues were devitalized by the force of the trauma. These were problems that could not be mastered by any perfection of aseptic technique. It is little wonder that the mortality from compound fractures of the femur in the first half of the war was 50%. It required two years of frustrating experience to appreciate that improvement in the treatment of war wounds depended upon resection of soft tissues so grossly damaged that they were incapable of protective reaction (debridement) followed by the use of antiseptic dressings (Carrel-Dakin solution, Eusol or B.I.P.P.). These measures constituted, in effect, a return to antiseptic surgery, and the earlier that debridement and antiseptic dressings were initiated, the better were the results, especially in such devasting infections as gas gangrene. Though it was not perfect, the control of infection proved to be the greatest surgical accomplishment of the 1914-1918 war. Some form of antisepsis was essential for such successful control of infection. This might just as well have been provided by carbolic acid as by Carrel-Dakin solution. Certainly the former would have been a much more convenient agent.

Many other surgical advances derived from the experiences of World War I. Some of the most important were those related to brain surgery, chest surgery, plastic surgery and abdominal surgery. Harvey Cushing, then rising to his zenith as the greatest neurosurgeon of his day, went to France before his country entered the war and, working with French and British units, exerted his skill with distinguished success in solving the problems of head wounds. His published studies on his cases have become classics. Chest wounds were of a magnitude not before seen by living surgeons and demanded new and bold measures of treatment. This marked the beginning of modern chest surgery. Abdominal wounds were frequent and severe. Their management involved the development of new techniques which profoundly influenced the future of abdominal surgery.

Wounds of the extremities frequently resulted in amputations and this in turn led to the necessity for development of suitable artificial limbs. It is to the credit of Canada that the measures taken to design and supply artificial limbs to military veterans were so successful that we acquired and still maintain a leading position in quality of prostheses provided for amputees. The Canadian Syme prosthesis and the Canadian prosthesis for hip disarticulation have become standard throughout the English-speaking world.

The influenza epidemic of 1917-1918 was so intimately related in time to the war as to seem a part of it, though of course their relationship was coincidental. Coming as it did at the end of the war, it involved many soldiers as well as the

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civilian population. The frequent complication of empyema presented a surgical problem not unlike that which followed gunshot wounds of the chest. Those who had developed surgical skill in this field by the care of chest wounds found ample opportunities for the continued application of their new knowledge. This vast amount of chest surgery, complementing the wartime experience with chest wounds, further strengthened the foundation of modern thoracic surgery. An early result was the introduction of the technique of intercostal drainage of empyema with negative pressure. This procedure quickly replaced the old method of rib section and open drainage which required a prolonged period for healing and led to obliteration of the pleural space, and at times distortion of the involved hemithorax.

## THE INTER-WAR PERIOD—1918-1939

The years between the two wars were filled with new developments. The lessons learned during World War I, the advances in bacteriology, immunology and biochemistry, the discovery that some human diseases are due to viruses, and development of the electron microscope, the application of new physiological knowledge to such surgical problems as thyroid disease and peptic ulcer, expansion of knowledge in the field of metabolism and co-ordination of surgical departments into a team, with the development of subspecialties and access to facilities for research, all combined to provide a stimulating atmosphere for major new advances.

Outstanding among these was the discovery of insulin by Banting and Best, in 1921. This was the work of a surgeon, and was important to surgeons because it demonstrated that practising surgeons could solve clinical problems by recourse to the experimental laboratory. Their discovery represented one of the most important developments of the period. There were many more clinical problems susceptible to solution by animal experiment, and these were vigorously investigated.

In this period too, there appeared a new approach to the science of anesthesia. Prior to the First World War, while surgery was vigorously perfecting its techniques and broadening its activities, there was little comparable activity in the field of anesthesiology. After the controversy of the 1890's over the relative merits and safety of ether and chloroform had subsided, the anesthetic agents universally used were ethyl chloride, ether, nitrous oxide and A.C.E. (alcohol 1 part, chloroform 2 parts, ether 3 parts), though there still remained some die-hard adherents to chloroform.

It was not until World War I that new developments in anesthesia began to accrue. In 1917 James Cotton of Toronto, investigating the reason for excessive postoperative vomiting after the administration of commercial ether, convinced himself that pure ether had no anesthetic properties and that the anesthesia which resulted from its use was due to the impurities it contained, of which the most potent was ethylene. He influenced certain pharmaceutical houses to distribute purified ether containing a fixed quantity of ethylene. His basic concept that pure ether was not an anesthetic agent was disproved in 1926 by the work of Wesley Bourne. However, Cotton's observations did direct attention to the anesthetic properties of ethylene. W. Easson Brown, in 1923, and Luckhart, in 1924, working independently, demonstrated that ethylene gas was a satisfactory anesthetic agent. In 1926, V. E. Henderson and E. H. W. Lucas of Toronto, searching for the cause of cardiac damage associated with propylene anesthesia, discovered that its isomer, cyclopropane, present as an impurity, was not the culprit, but instead was a powerful anesthetic in its own right, with many valuable properties. Thereafter, cyclopropane enjoyed widespread use for many years.

The successful introduction of intravenous anesthetics arose from the development of the barbiturates. The period of greatest and most productive activity in this field was between 1929 and 1934, culminating in the development of sodium thiopental by Lundy, in 1934. This intravenous anesthetic agent, so widely used today, has the great merits of rapid induction, easy control and rapid excretion. It has eliminated much of the fear and danger of anesthesia.

A pioneer in the use of intratracheal anesthesia in Canada was C. H. Robson of Montreal, who developed his technique for introduction of the catheter by finger-tip guidance, in 1913. He employed this procedure in military hospitals during the First World War and perfected it when he came to Toronto in 1919. For many years Robson was the sole exponent in Toronto of anesthesia administered by intratracheal intubation. Magill's tubes which were inserted through the nose and then passed blindly through the larynx were introduced in 1929. The modern technique of introducing an endotracheal catheter by means of a laryngoscope derives from Chevalier Jackson's perfection of the direct-vision laryngoscope and its adaptation to the introduction of intratracheal tubes by Kirstein in 1895. Intratracheal insufflation of anesthetic gases has become an essential technique in pulmonary surgery, particularly with the development of inflatable cuffs which permit occlusion of the trachea and main bronchi.

A most important adjunct to modern anesthesiology has been the use of curare which was introduced in 1942 by H. R. Griffith and E. G. Johnson of Montreal. The particular value of this drug lies in its capacity to induce muscle relaxation. When combined with a gaseous anesthetic administered through an intratracheal tube, it permits controlled respiration even in the presence of profound muscular relaxation, a great asset in many aspects of surgery. Curare, as first used by Griffith and Johnson, was in the form of the purified and

standardized arrow poison of South American Indians. It has since been synthesized and is available in modifications which are superior to the natural product.

Among the greatest advances initiated in the period between the world wars, and still continuing, have been those in the field of cardiovascular surgery. Some of the fundamental research which made these advances possible is the result of Canadian effort. Vascular and cardiac surgery had been practised for at least two centuries. John Hunter's treatment of popliteal aneurysm (1785) marked a great advance in vascular surgery, and the work of Rudolph Matas (1860-1957) on arteriovenous aneurysms and cardiac and vascular wounds, throughout his long and productive lifetime, added much to the knowledge of this highly technical branch of surgery. For many years, however, the success of vascular surgery was seriously impeded by the seemingly insuperable difficulty of controlling or preventing blood coagulation during and after such operations. This major problem was eventually overcome by the introduction of the anticoagulants, heparin and dicoumarol. Between 1933 and 1936, Charles Best and his co-workers devised improved techniques for collecting and concentrating heparin in a stable form suitable for clinical use. Gordon Murray, in 1936, using heparin intravenously, perfected many of the details whereby vascular and cardiac surgery could be performed safely, quickly and without the complication of clot formation. In 1924, Schofield, working at the Ontario Veterinary College in Guelph, established the fact that the disorder known as red-water fever in cattle was a hemorrhagic disease due to a profound disturbance of the clotting mechanism of the blood which was manifested by massive hematuria and fatal hemorrhages from wounds such as those incurred in the process of dehorning. Schofield was able to demonstrate that this hemorrhagic state resulted from the consumption of mouldy sweet clover hay, the toxic component of which was cumarin. This substance, first isolated from sweet clover, and later synthetized as coumarol, is now widely used in the practice of medicine as dicoumarol, so well known for its efficacy in the prevention and treatment of thrombosis. Much of modern cardiac and vascular surgery would be impossible without the aid of these anticoagulant agents, heparin and dicoumarol.

Hypothermia had been used for a century in the form of refrigeration anesthesia. Local areas of the body were reduced in temperature until they were insensitive or even frozen, so that minor surgery or even amputations could be performed. Temple Fay, in 1938, introduced total body refrigeration to control the pain of patients with hopeless carcinoma. It remained for William Bigelow of Toronto to apply the principle of hypothermia to cardiac surgery, as well as to certain surgical procedures on the brain and the extremities, by demonstrating that, as a result of reduction of body temperature, the oxygen requirement of the body, and particularly of the brain, could be substantially reduced, permitting interruption of the circulation for sufficient time to perform intracardiac operations or to undertake massive vascular transplants. Bigelow's studies on hypothermia have led him also to investigate the phenomenon of hibernation and he is still engaged in this problem.

Additional new techniques which have contributed to the dramatic advances in cardiovascular surgery in recent years include the transplantation of arterial, venous and fascial grafts, the use of substitution grafts such as teflon, and the introduction of apparatus to permit mechanical bypass of the cardiac circulation by extracorporeal circulation maintained with a pump.

Thoracic and pulmonary surgery also became important specialties in the period between the two world wars. Experience with war injuries of the chest in World War I taught surgeons that bold opening of the chest was necessary to remove clot and foreign bodies and that this procedure could be performed without fatal results. The influenza epidemic at the end of the first war produced thousands of cases of a particularly serious type of empyema. The surgical management of these patients by intercostal catheter drainage with negative pressure was the first advance in the management of the problem which had occurred in decades. Evarts Graham first established his reputation as a thoracic surgeon in 1920 with his paper on empyema as observed in U.S. Army camps. The surgery of pulmonary tuberculosis commenced when it was realized that pneumothorax could not always achieve the desired collapse of the lung because of massive adhesions. This led to development of techniques for segmental thoracoplasty; to thoroscopy and section of pleural adhesions by cautery, and to extrapleural collapse of the lung. As experience broadened and as improved anesthetic agents became available for intratracheal administration, lung resections were attempted. At first these were confined to lobectomies and partial resections for bronchiectasis, localized tuberculosis or tumours; later, total pneumonectomy was introduced especially for pulmonary carcinoma. To Evarts Graham goes the credit for the first successful total pneumonectomy for pulmonary carcinoma. As long as Dr. Graham was alive, his grateful patient (a doctor) telephoned him every year on the anniversary of the operation.

Norman Shenstone and Robert Janes of Toronto, Edward Archibald of Montreal and Ross Robertson of Vancouver are Canadians who have been in the forefront of these advances in chest surgery, and their work is internationally recognized.

The great increase in incidence of bronchial carcinoma has been a striking feature of this period and the evidence advanced by Evarts Graham that this is related to cigarette smoking has been an important piece of clinical research.

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In Canada, the specialty of plastic surgery developed from the necessity of dealing with the mutilating injuries of the first war, particularly facial injuries and disfigurements. During that war, a joint plastic and reconstruction unit, common to Great Britain, Australia, New Zealand and Canada, was established in Sidcup. Fulton Risdon and C. W. Waldron were the Canadian members of the staff. When the war ended, the Canadian unit was established at Ste. Anne de Bellevue and transferred later to Christie Street Hospital, Toronto. C. W. Waldron left Canada shortly after this to join the staff of the Mayo Clinic. Fulton Risdon continued to direct the plastic unit at Christie Street Hospital. He was the first Canadian to devote himself exclusively to plastic surgery and is the founder of this specialty in Canada.

The complexity and multiplicity of war injuries were major factors in fostering the new developments in plastic surgery. The skin-grafting technique of Ollier and Thiersch was improved and utilized to cover areas denuded of skin, and to diminish the contracture of scarred areas by means of inlay grafts. In addition, a major elaboration of the principle of pedicle skin grafting developed, based upon the ancient Indian and Italian rhinoplasties. Burned patients presented special problems in metabolism, fluid and electrolyte balance, infection and skin coverage, which stimulated active interest and research. A vigorous new specialty arose which, by reason of the skill and dexterity it requires, has won well-deserved recognition. Its position was strengthened by the work of Kanaval and Bunnell in hand surgery, a field which has been taken over in many centres by plastic surgeons since it involves intricate problems in skin and soft tissue repair as well as reconstruction of the framework and motor units of the hand.

Other fields of surgery, too, enjoyed major advances during the inter-war period. Gastrointestinal problems were vigorously investigated. The nature of peptic ulcer was clarified, much helped by Cushing's observation already mentioned, and its treatment was rationalized and greatly improved. The metabolic etiology of certain forms of cholecystic disease was unravelled and their surgical treatment perfected. Pancreatic diseases yielded to surgical treatment, stimulated to a large degree by Allen Whipple, who devised practical techniques for resection of the head of the pancreas for carcinoma. A Toronto group recognized for the first time a case of hyperinsulinism due to adenoma of the islet cell tissue of the pancreas and recorded its spectacular cure by resection of the tumour. Techniques for dealing with malignancies within the abdomen were improved.

Genitourinary surgery advanced rapidly. Cystoscopy became a more valuable procedure as the result of improvements in instruments. The introduction of intravenous pyelography simplified urological diagnosis and at the same time provided a reasonable assessment of renal function. Transurethral prostatectomy was introduced. Towards the end of this period the advent of sulfonamides afforded more adequate control of renal and bladder infections than had ever before been possible. A new concept of renal tuberculosis developed from studies conducted at Christie Street Hospital and the Hospital for Sick Children, Toronto.

## THE 1939 - 1945 WAR

The 1939-1945 War also exerted a profound influence on surgery. The outstanding achievement in this period was the great improvement accomplished in the management of war wounds. The lessons learned in World War I concerning wound treatment were not too clearly understood, nor was their importance fully appreciated. The impression existed that these techniques were of value chiefly for grossly contaminated wounds caused by shell fragments. Moreover, the Carrel-Dakin technique was difficult to carry out. The equipment was somewhat complicated and required trained personnel for its proper use. Carrel-Dakin solution required daily titration and frequent renewal to ensure that it retained its potency. By the time the Second World War commenced, formal Carrel-Dakin treatment had been virtually abandoned. Debridement of compound fractures was still used in a simplified fashion and it is true that antisepsis was practised by certain surgeons in dealing with specific problems. Fraser Gurd of Montreal was using BIPP with success, particularly in infected abdominal wounds. Harris in Toronto was using carbolic acid (Keith's dressing) to prevent secondary infection in tuberculous sinuses. Also, stable chlorine solutions became available to replace the unstable Dakin's solution and these proved valuable as surgical dressings, particularly for superficial wounds such as burns.

Immediately before the onset of the 1939-45 war, three events occurred which improved the mastery of infection and therefore enhanced the successful management of war wounds. These were the introduction of sulfonamides, the advancement in knowledge concerning the streptococcal group of organisms, and the application of the closed plaster treatment of war wounds developed by Trueta in Barcelona during the Spanish Civil War.

The sulfonamides first became available in 1936 and quickly demonstrated their value in the treatment of respiratory and urinary infections. They were particularly effective against streptococci. New and improved forms of these drugs proved valuable in the treatment of infected wounds, particularly in the prevention of infection in compound fractures. By the time the war broke out, experience had demonstrated that they had a profoundly beneficial effect in the treatment of a variety of infections.

Prolonged studies of the streptococcal group of organisms, which came to fruition in the latter part of the inter-war period, demonstrated that the

common habitat of these bacteria was the nose and throat of human beings. Besides initiating respiratory diseases, they could contaminate wounds directly, through coughing, sneezing or talking in close proximity to the wounds, or indirectly from contaminated hands, dressings, clothing, bedding or instruments. As demonstrated by Ronald Hare in the Connaught Laboratories in Toronto and by others, the entire equipment, and indeed the very atmosphere of a hospital ward, could readily become contaminated by these organisms. This was especially true in the winter when clinical streptococcal infections were rife. In January of 1926, the operating rooms of the Children's Hospital in Toronto had to be closed because of an abrupt outbreak of streptococcal wound infection in "clean" cases. Fifty patients were so infected; two of these children died and several others developed "surgical scarlet fever". It took time to demonstrate fully the menace of streptococci and still longer to appreciate the measures necessary to prevent streptococcal infection of wounds, particularly compound fractures. These measures involved elimination of the source of streptococci when this was possible, and continuous covering of wounds by protective dressings or preferably by early skin closure. Part of the merit of Winnett Orr's closed plaster treatment of osteomyelitis was the exclusion of secondary streptococcal infection.

Immediately before the outbreak of the Second World War, Joseph Trueta published a small monograph entitled "The Treatment of War Wounds and Fractures with Special Reference to the Closed Method as used in the War in Spain" (1939). It recounted his experience in the management of compound fractures during the siege of Barcelona. By early operation, wide exposure, adequate debridement, drainage provided by gauze packing to keep the wound open and then enclosure of the whole limb in a plaster spica, he was able to achieve the astonishingly low mortality rate of 0.5% (6 deaths in 1150 patients with compound fractures) and a very low incidence of gas gangrene and other infections. Early secondary closure of the wound was possible. Trueta's method was born of the necessity of managing large numbers of cases in a limited time and with limited staff, and the need to provide for early transportation. Though at first his work was viewed with some skepticism (it seemed too good to be true), it proved to be substantially what he claimed it to be, a major improvement in war surgery. Its acceptance was facilitated by experimental work which Trueta conducted at Oxford during the war; this proved that the closed plaster treatment, if properly carried out, had two important merits: it excluded secondary infection from the wound and, by splinting the soft tissues, it greatly facilitated the development of local barriers of defence against the spread of infection.

These three advances in the treatment of wounds were available when the war broke out. A fourth, of even greater importance, developed during the first two years of the war. This was Florey's expansion of Fleming's discovery that the mould *Penicillium notatum* produced a substance which killed staphylococci. Florey extracted the material from the culture medium on which the mould had grown. The brown powder so produced was penicillin, the discovery of which was an outstanding landmark in the history of man's fight against infection. A small quantity was available for the North African and Italian campaigns in 1943 and immediately proved its value. Ample supplies were available for the Normandy landings in 1944 and this drug in conjunction with the closed plaster technique and adequate facilities for early treatment revolutionized the management of compound fractures in war.

Nothing is more characteristic of war than wounds; nothing epitomizes the quality of war surgery so well as does the management of war wounds, and of these, compound fractures present the gravest problems. For these reasons it may be said with justification that the outstanding advance in surgery during the 1939-1945 war was in the mastery of the problems of treatment of compound fractures. This was accomplished by a precise surgical technique involving early operation, wide exposure and wide incision of fascia to relieve tension, adequate debridement to remove all devitalized soft tissues and all foreign bodies, drainage maintained by packing the wound open with gauze, closed plaster fixation and early secondary suture; and by the new powerful antibacterial agents, penicillin and, to a lesser degree, the sulfonamides.

There were, of course, other important surgical achievements during the 1939-1945 war. The list is long: the treatment of shock by blood and blood substitutes; the development of blood banks and blood distribution services; the processing of blood plasma and serum to powder; the management of amputations and the development of new types of prostheses such as the suction socket for above-knee amputation, the Syme prosthesis and the prosthesis for disarticulation of the hip; vascular surgery in the field to save limbs; the establishment of centres for neurosurgical and plastic cases; field surgical units to ensure early and adequate surgical treatment of wounds with a minimum of transportation; elucidation of the crush syndrome and kidney dysfunction which follows impairment of renal circulation.

## THE POST-WAR PERIOD — 1945-1960

Since the Second World War, the advance of surgery has been a steady one. Probably the most significant development has taken place in the field of antibiotics, an outcome of the discovery of penicillin. Literally the whole world has been searched for moulds which possess antibiotic properties. From this immense search a few have been found which have yielded highly effective

antibiotic agents. These have resulted in further mastery of infections, many of which formerly were treated by the surgeon. Penicillin has provided an effective cure for the two major venereal diseases, gonorrhea and syphilis. Streptococcal infections have disappeared from the wards of hospitals. Otitis media and its complications are now rare. Osteomyelitis responded dramatically to the combination of penicillin and sulfonamides and for a time could be cured without operation. Then, unfortunately, resistant strains of staphylococci made their appearance and penicillin lost much of its efficacy as an antistaphylococcal agent. This complicated the situation until other effective antibiotics became available.

A dramatic outcome of the development of antibiotics has been the near mastery of tuberculosis, though not all of this success has been due to streptomycin and other antituberculous agents. Improved programs for the recognition of tuberculosis in its early stages by mass survey techniques, early hospitalization, early treatment and vast expansion of the surgical eradication of all forms of tuberculosis have all played their part in reducing the problem to the point at which sanatoria in Canada are being closed or transferred to other uses. There is a real possibility that within ten years tuberculous infections will constitute but a minor problem. Of all the forms of this disease which have been benefited by antibiotics, in none has the improvement been more dramatic than in the fields of bone and joint and renal tuberculosis. Fifty years ago one of the most dreaded complications of bone and joint tuberculosis was the implantation of secondary infection into a tuberculous bone abscess. There was a time, indeed, when this complication was fatal. Some protection against the implantation of secondary infection could be provided by such antiseptics as carbolic acid in glycerine, but this was not always effective. It was not until the sulfonamides were introduced that some control over established secondary infection was obtained and this was greatly enhanced when penicillin and streptomycin became available in 1945. Thereafter it was not uncommon to observe healing of secondarily infected tuberculous sinuses which had existed for years, or even for decades. In some early cases of tuberculosis of the hip and knee it is now possible to obtain a cure with a normally functioning joint by antibiotic therapy alone. When operation is necessary, it is much safer and much more successful with the protection provided by antibiotics. Renal tuberculosis, which once was incapable of cure after it had reached a certain stage, can now often be cured by streptomycin and its associated drugs. The value of antibiotics in the treatment of tuberculosis is of great importance in areas such as India and the Orient where the incidence of the disease is high, living conditions are crowded and poverty is universal. In such countries, facilities for hospitalization are inadequate and treatment of joint tuberculosis by fusion is unwise, because ankylosed joints interfere with earning a living. When surgery is necessary, bolder approaches and a shorter period of hospitalization are now possible with the protection afforded by antibiotics. Hodgson of Hong Kong has operated upon 200 patients with dorsal Pott's disease by a transpleural approach without complications and with great success.

A postwar development of great importance has been the expansion of knowledge of virus infections. The viral etiology of many diseases has been recognized, and new and successful methods of growing viruses have been devised. These advances in virology are leading to the effective control of poliomyelitis, a development with considerable influence on the field of orthopedic surgery. The viral etiology of this disease had been recognized for some time and several strains of viruses causing paralytic manifestations had been isolated. The development of a protective poliovirus vaccine was delayed by the problem of culturing the virus in quantities sufficient to permit its use in large-scale immunization programs. The Connaught Laboratories in Toronto contributed to the solution of this problem by the development of a synthetic medium for culture of tissue cells. This permitted the growth of poliovirus on a large scale, in tissue cultures of rhesus monkey kidney cells. The poliovirus vaccines so produced bid fair to contribute materially to the eradication of poliomyelitis.

It appears that we are on the threshold of further advances in virology which may explain the nature of many presently obscure clinical entities. Techniques for recognition of viral diseases are rapidly improving. There is an active interest in the possibility that at least some forms of malignant disease may be of viral origin.

An important contribution to the expansion of knowledge of viruses was the development of the electron microscope in Germany by Knoll and Ruska, in 1932. The first electron microscope in North America was constructed in 1938 in the Department of Physics of the University of Toronto by Professor Burton and his associates, Prebus and Hillier. For many years its use in histological preparations was handicapped by lack of satisfactory techniques to prepare sections of sufficient thinness. This difficulty has been solved only in the last decade by the use of glass blades to cut specimens in extremely thin films after mounting in a plastic block. As a result of these developments in electron microscopy, extraordinary advances have been made in the knowledge of the minute structure of cells and in the study of viruses. It is interesting to record that in October 1960 the German engineer Ruska and the physicist Hillier received the Lasker award in Medical Research for their contributions to the development of the electron microscope.

Cardiovascular surgery, too, has made immense strides in recent years. After the introduction of the procedure for ligation of patent ductus arteri-

osus by Gross in 1939, techniques were developed for the complicated readjustment of vessels necessary to improve such congenital abnormalities as the tetralogy of Fallot and coarctation of the aorta. The availability of heparin and dicoumarol permitted the performance of such operations free from the hazard of intravascular clotting. There followed immediately a great expansion in operations upon blood vessels which has now reached a point at which resections of great lengths of major arteries such as the aorta, and their replacement with cadaver arteries or with tubes woven of synthetic fibres are common procedures. Vascular banks exist for the preservation and storage of blood vessels to be used for this purpose. Bypass operations using venous or arterial grafts restore circulation to parts beyond an obliterated main trunk. Major improvements in the technique of arteriography have facilitated the diagnosis of many arterial lesions.

The possibility of performing intracardiac operations for the repair of congenital or acquired defects required a technique which would permit the cardiac flow of blood to be interrupted or diverted for a sufficient length of time to permit completion of the operation without simultaneously causing irreparable ischemic damage to vital organs such as the brain, kidney and the heart itself. The two solutions to this problem currently employed are the use of controlled hypothermia, which reduces the oxygen requirement of the body in proportion to the reduction in body temperature, and the introduction of extracorporeal circulation, in which a pump diverts all the blood from the heart and maintains its flow through the lung and the peripheral vessels. Both have been successful in extending the field of intracardiac surgery.

The availability of radioactive isotopes resulting from great advances in atomic physics has provided agents for more accurate diagnosis and treatment of disease. Radioactive iodine has proved valuable in the management of certain aspects of thyroid disease. Radioactive phosphorus is a useful agent in the investigation of bone metabolism, though the interpretation of the findings of such studies has been tantalizingly difficult. The diagnosis and localization of brain tumours has been improved by their selective absorption of radioactive arsenic, copper and yttrium.

The therapeutic use of hormones in the management of certain surgical problems, notably carcinoma of the breast and of the prostate, has been a major advance. To be able to halt the progression of breast cancer and to hold it under control without major surgery is a dramatic experience and seems to offer promise of increased knowledge of the nature of cancer and possibly of the control of its course.

Powerful radioactive elements have also led to improvement in the radiation therapy of cancer, chiefly in the form of cobalt and cesium bombs which were developed first in Canada. With these agents it is possible to project a narrow but powerful beam of radiation which, when properly manipulated, can be concentrated on a deep lesion with little damage to the skin and soft tissues and with greatly increased effect upon the carcinomatous lesion.

In orthopedic surgery, since the last war, great advances have been made in knowledge of the structure and physiology of bone and connective tissues. Of all the fundamental tissues of the body, bone has been one of the most difficult to understand. To a lesser extent this has been true of other connective tissues but it is especially true of bone where the distinctive qualities of rigidity and strength are due to large masses of calcified intercellular substance in which the cells and blood vessels seem lost. The wood-like quality of bone invited surgeons to embark on procedures not unlike those of the cabinet maker and with tools derived from his craft. The spectacular success of these empirical procedures retarded for decades any really serious study of bone as a living tissue. Experience seemed to demonstrate that bone could be handled like the cabinet maker's wood. What really was demonstrated was that bone is a tissue so vitally alive that it can withstand almost any insult. It is true there had been many histological examinations of healing fractures and investigations of the fate of bone grafts, but these merely confirmed histologically what was already known from clinical experience, viz. that fractures unite and bone grafts become incorporated into the bones with which they are in contact. The careful histological studies of A. W. Ham, in Toronto, did much to provide a clear picture of the histology of bone and knowledge of its physiology. In the last decade, research has increased our knowledge of bone as a living organ. Much has been learned but there is still much of the mystery to unravel. It is a healthy sign that orthopedic surgeons are concerned with fundamental research into the nature of the tissues with which they work.

On the technical side, advances have been made by Trueta and others in our knowledge of the blood supply of bone, especially that of the head of the femur, in health and disease. Intramedullary nailing of fractures of long bones was placed on a new improved basis by Küntscher in the latter half of the 1939-1945 war. Hey-Groves devised this technique first in 1914, but the time was not ripe for its acceptance and his technique was not simple. In 1945 an improved technique together with the availability of penicillin and the great number of fractures of the femur requiring treatment led to immediate acceptance of Küntscher's technique and extension of the principle to most other long bones. It has proved a valuable addition to our methods of fracture treatment.

Another important postwar development was the replacement of the damaged half of joints by a plastic or metal substitute. The principle was

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introduced in 1956 by the Judet brothers, who used an acrylic prosthesis to replace the femoral head in the treatment of osteoarthritis of the hip. Within certain limits this has proved a very valuable procedure, though both the design of the original prosthesis and the material from which it was made have had to be changed.

In this postwar period the work of orthopedic surgeons has been modified by many changing factors. The enormous increase in road accidents has resulted in an increasing proportion of traumatic surgery. The management of these problems is essentially similar to that of war wounds, and the experience gained in the last war is directly applicable to their treatment. Other fields of orthopedic surgery have contracted, notably those of tuberculosis of bones and joints, poliomyelitis and osteomyelitis, in each case because of improved ability to control the infection.

Knowledge of certain obscure orthopedic problems is expanding. Included among such disorders are Legg-Calvé-Perthes disease, congenital dislocation of the hip and such characteristic osseous lesions as osteoid osteoma, aneurysmal bone cyst and fibrous dysplasia. Work in this field has been greatly benefited by recent research on the histology and physiology of bone. A new concept of congenital abnormalities has arisen with the demonstration that certain of these conditions are not genetic in origin but are the result of intrauterine trauma or infection. They are congenital defects in that they are present at birth but are not the result of defective genes. In 1941, Gregg reported congenital deficiencies, chiefly in the form of deafness and blindness, in children whose mothers had suffered from rubella in the early weeks of pregnancy. Duraisnami's work (1952) is of particular interest to orthopedic surgeons because he demonstrated that metabolic trauma to the embryo (insulin injection) can produce profound skeletal deformities. This is a wide field for future investigation.

This attempt to record the developments of surgery in the last fifty years is rambling and incomplete. But if it conveys the impression that this period has been filled with a ferment of new ideas and, despite the tragedy of two world wars, has succeeded in encompassing more progress than any comparable period in history, it will have served its purpose.

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## THE CANADIAN MEDICAL ASSOCIATION: THE PAST FIFTY YEARS

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THE OCCASION of the Golden Jubilee of the *Canadian Medical Association Journal* offers a good opportunity to consider the Association as a whole since 1911. At that time we had a tangible link with the founding fathers, because Sir Charles Tupper, the first President, was alive at the age of ninety. The President was Dr. G. E. Armstrong and the General Secretary, Dr. E. W. Archibald, both of Montreal.

From this distance the affairs of the medical profession appear simple and uncomplicated. State medicine was occasionally still employed as a synonym for public health, health insurance was dimly comprehended as a system which the firebrand Lloyd George was promoting for the underprivileged classes in Great Britain, and income tax was unknown in this country. Despite the idyllic view down the vista of fifty years, our able and energetic forefathers had their problems and the national organization of doctors was coping with them to the best of its ability.

There were just over 7000 doctors in this country in 1911, and approximately 1400 of them were members of the C.M.A. Membership was linked in the minds of many with attendance at the Annual Meeting, and the consequent uncertainty of decision to contribute the annual fee of $5.00 made budgeting difficult. Among the major undertakings which occupied the Association was the decision to establish its own Journal, and the story of the preliminary struggle is related elsewhere in this issue. Concurrently, the campaign of forty years for the establishment of a uniform standard of medical qualification through the Medical Council of Canada was being brought to a successful close by Sir Thomas Roddick, the only man ever elected Honorary President for life. The state of clinical medicine was reflected in committee activities for the provision of pure water supplies to prevent the spread of enteric infections and in the C.M.A. Milk Commission, which set the stage for the elimination of bovine tuberculosis. The establishment of a Federal Department of Health was being urged and better facilities for the collection of vital statistics was a current project. The report of the Association's Committee for the Prevention of Tuberculosis was "decidedly unfavourable". Two years later, in 1913, short shrift was given to a resolution proposed by Dr. F. N. G. Starr who advocated the establishment of a non-teaching college for the conferring of degrees in the specialties, when Dr. Adami rose to a point of order to the effect that such a motion must first be presented to the Executive Council.

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This incident is mentioned to record the earliest beginnings of an idea which has found fruition in the Royal College of Physicians and Surgeons of Canada and also to illustrate the rivalry which existed between representatives of the two principal medical centres of that day. I have heard it said that the C.M.A. was operated for many years as a private club, the members of which were the teachers at McGill and Toronto. Indeed, the organization was not very representative or democratic, but its structure provided little scope for those features which we believe to be so important. The Canadian Medical Association was national in name only, and the only relationship which peripheral medical organizations—local or provincial—had with it was by means of ill-defined affiliation. In 1911 the Ontario Medical Association was the only provincial body which was affiliated, and the allegiance of the doctors of certain areas was actually closer to the B.M.A., of which they constituted branches.

However, the stirrings of true Canadian nationalism were shortly evident. The Alberta and Manitoba Medical Associations affiliated, the Maritime Medical Association voluntarily disbanded and soon the existing nine provinces brought their associations and societies into a kind of relationship with the C.M.A.

The governing body of the Association was called the Executive Council. It consisted of fifteen persons elected by the Annual Meeting. If a member of the outgoing Council were present, his re-election was almost automatic. In the minutes of the Forty-seventh Annual Meeting, held in Saint John in July 1914, the election procedure is described as follows: "The election of the fifteen Association members to the Executive Council was then proceeded with. The following seven of the retiring Council, being present, were nominated individually: Drs. White, MacNeil, Starr, Mader, Hutchison, and Thomson. The President [Dr. Murray Maclaren] considered that it was not customary to elect these in a body. Twelve more were then nominated, rendering a ballot necessary. Considering the time it would consume, many suggestions were made and it was finally moved, seconded and carried that the nineteen names written on slips of paper be put into a hat and that the President draw out fifteen slips, those whose names appeared thereon being declared elected. This was accordingly done. The seven whose names appear above were drawn and together with the eight following were elected: Dorman, McDougall, Stewart, Anglin, Kidd, McPhedran, Primrose, Birkett, Turner and McCallum. These fifteen with the delegates from Ontario, New Brunswick and British Columbia Associations constitute the Council for the ensuing year." My predecessor in the office of General Secretary, Dr. W. W. Francis, probably recorded these proceedings and, though his mathematics will not stand up to close scrutiny, the Association had provided itself with an Executive Council, the members of which were to lead the Association into World War I and hold office until their successors were elected in 1917.

A revision of the Constitution and By-laws was undertaken by a committee and presented to the Annual Meeting of 1919, held in Quebec. The proposals did not meet with the approbation of that great constitutionalist, the late Dr. Heurner Mullin of Hamilton, for he led the attack on them and succeeded in having them referred back. The terms of a resolution proposed by Dr. Mullin, "That the Executive Council be asked to appoint a committee to assist in and to further a more complete organization of the profession of the Dominion through the medium of the Provincial Associations now constituted and others which should be encouraged to be organized", clearly indicate that he was promoting a more representative organization than had previously existed.

This concept was reflected in the new Constitution and By-laws adopted at the 1920 Annual Meeting in Vancouver, which provided for "Branch Associations. The Provincial Association in each province may by special resolution of such Association become a branch of the Canadian Medical Association by subscribing to its Constitution, By-laws and Code of Ethics and by securing the approval of the Council. They shall submit a copy of their Constitution and By-laws and such amendments as may be made from time to time."

In this significant organizational step the Council of the Association was established as a body primarily representative of the Provincial Branch Associations.

The real turning point in the affairs of the Canadian Medical Association occurred at the Annual Meeting in Halifax, in July 1921. In addition to rescuing an organization which was on the financial shoals by a heartening demonstration of faith, courage and cold cash, the members present approved a Plan of Reorganization which placed the Provincial Associations in proper relationship to the C.M.A. and made the latter for the first time a representative body. More significant, however, than all the fine talk of a new outlook, was the power granted to the new Executive Committee to appoint a paid full-time Associate Secretary. They apparently lost no time in closing the deal with young Clarence Routley, because his name appears on the very next page of the proceedings in his capacity as Associate Secretary.

The new look of the C.M.A. as a national organization proceeded by fits and starts, but in 1924 a further revision of the By-laws aided the concept of unity. The geographical difficulties with which we still contend were aptly described by Dr. D. A. Stewart: "Shoulder to shoulder is rather hard to manage with one shoulder in Alberta and another in New Brunswick."

The efforts and the enthusiasm of Dr. J. S. McEachern of Calgary were probably the most important elements in welding the Association into

its present form. During his presidency in 1934, he made the concept of federation a crusade, the fervour of which served to reassure the sceptical provinces, to quell the fears of loss of autonomy, to stimulate the indolent and to inspire his listeners with a measure of his vision. It took five years (1934-1939), however, to achieve the federation of each of the provincial medical associations to their new relationship as Divisions of the Canadian Medical Association. At the Annual Meeting in 1940 the culmination of the organizational realignment was reported in the following terms:

"It would seem likely that the five-year period from 1934 to 1939 will stand out as one of the most important epochs in the history of the Association. The foundations for a truly national medical organization have been well laid. Essential elements guarding provincial autonomy while making for national cohesion have been carefully woven into the Constitution and By-laws. It now remains for the profession in all the provinces of Canada to build upon this foundation a Canadian Medical Association fully capable of performing successfully all the duties and functions which should devolve upon a medical association."

To the average member who is not particularly interested in the minutiae of organizational structure, the accomplishment may not seem very impressive. To the Divisional executive officer who is close to the realities of the day-to-day decisions that must be made in a wide variety of health issues, the functioning of a national organization may appear ponderous and slow. To one who is sufficiently patient to seek to achieve a national outlook on any given question and who is tolerant of the processes of democracy, the federated structure of the C.M.A. represents an organization which is effective and one which elicits favourable comment from other workers in the complex Canadian scene. The General Council has truly become the Parliament of Canadian medicine.

Closely paralleling the development of representative government in the Association, the range of its committee activities greatly increased in scope and importance. The rapid advances in the science of medicine have been eagerly accepted by both public and profession alike, and it has followed inevitably that there should arise the concept that the abundant benefits of personal health services should be available to all. The advances in science have been accompanied by significant increases in expenditures for health care in both the public and private sectors of the economy. This development of our times has made it necessary that doctors collectively should devote much thought to the marketing of their services.

Health insurance has become the central problem of the organized medical profession throughout the world, and in Canada it has for many years occupied the centre of the stage in the deliberations of the Canadian Medical Association. During the period under review, two world wars, with their subsequent stimulation of the economy, have bracketed a period of depression such as this country had not previously experienced. These factors have had their influence on the studies and conclusions of successive Committees on Economics and it is important to realize that the policy pronouncements of the C.M.A. have been made in the contemporary atmosphere of the state of the nation.

Brief references to health insurance, mainly commenting on the situation in Great Britain, appeared in the records of the Association and its Journal as early at 1919-1920, but the first serious consideration of the matter occurred in 1929 when the Committee on Economics reported a resolution of the Ontario Medical Association recommending a government commission to study health insurance and to suggest ways of achieving adequate medical services. Such a commission had been established in British Columbia and its report was the precursor of the abortive attempt to introduce a measure of health insurance in that province in 1934-1935. Meanwhile, the devastating effects of the depression were everywhere evident and in 1934 the Committee on Economics presented its "Plan for Health Insurance in Canada," which embodied seventeen principles upon which this or any other plan should be based.

In Ontario a long campaign culminated in 1935 in the establishment of the Medical Welfare Plan, by which a token payment from public funds was made to the Ontario Medical Association for the medical care of some 350,000 recipients of relief. The significance of this arrangement should be appreciated because it represents the first occasion in Canada when funds to support health insurance for a substantial proportion of a population were turned over to a voluntary medical body for administration and distribution. Similar plans followed in four other provinces, the most recent in Manitoba in 1960.

The emergence of voluntary plans of prepaid medical care for self-supporting members of the community represents the effort of the medical profession to answer the growing need for a means of insuring against the cost of medical services. Beginning in 1937 with Associated Medical Services and Windsor Medical Services, the western half of Canada was soon served by plans providing comprehensive medical benefits rendered on a service basis, in each instance sponsored and supported by the organizations of the profession. The concurrent and parallel development of Blue Cross plans of hospital care insurance was an important factor during this period.

A study of the operation of health insurance plans in the United Kingdom and in continental Europe was undertaken by the General Secretary in 1937 and the report of the Committee on Economics in 1939 embodies many of his observations.

The outbreak of war in 1939 impeded the progress of studies and projects in the Association,

but the Government of Canada in 1942 created the Advisory Committee on Health Insurance, under the chairmanship of Dr. J. J. Heagerty, to proceed actively towards a measure of health insurance for postwar implementation. A committee of seven persons was selected by the C.M.A. to work closely with the Advisory Committee and there was actually evolved a Draft Bill of Health Insurance designed to provide the model for Federal and provincial enactments. In 1943 a special meeting of the General Council was called to consider the attitude of the Association towards what appeared to be the certainty of legislative action. The Association went so far as to "approve the adoption of the principle of health insurance" and restated twenty principles which were considered to be the basis for the participation of the profession.

The progress towards health insurance by legislation was temporarily halted in 1945 when the Dominion-Provincial Conference on Reconstruction failed to agree on fiscal matters and the Federal offer of aid to the provinces was withdrawn. The interest of the government was, however, not long in reasserting itself. In 1948 the Government of Canada, after consultation with the C.M.A., announced that ten National Health Grants would be offered to the provinces. It is significant that the Prime Minister described these grants as "being fundamental prerequisites of a nation-wide system of health insurance".

In 1949 the Association issued a Statement of Policy on health insurance which stressed its support of the voluntary plans of prepaid medical care, the right of every citizen to insure under them and the obligation of the state to provide the premiums of the needy. The Statement also declared hospital care insurance to be the "first and most urgent" stage of a comprehensive health plan.

The medically sponsored plans of prepaid medical care, which had operated as independent local agencies, were called together under C.M.A. auspices to a series of meetings which resulted in the formation in 1951 of the national organization now known as Trans-Canada Medical Plans.

The interest of governments in various aspects of health insurance continued to be evident, and in 1955, after two years of study by the Committee on Economics, the General Council adopted a further statement of policies and principles on health insurance in Canada. In this document for the first time the Association faced up to its role in the event of government participation in the universal extension of health insurance to all citizens.

In the meantime, both Federal and provincial governments were negotiating the terms of a universally available plan of hospital care insurance. The passage in 1957 of the Hospital Insurance and Diagnostic Services Act led to the signing of agreements with all provinces for this important element in the total range of health insurance. It is evident that the success of the hospital insurance plan has had considerable influence on the creation of a demand for a tax-supported system of medical care insurance.

In 1949 there was brought into the federation which we call Canada the tenth province, Newfoundland. Incidental to this union we have acquired a co-partner which for many years has solved many of its problems in the field of health by governmentally administered plans. The provision of medical care to the scattered population of the Newfoundland outports has been since 1935 undertaken through the Cottage Hospital system. The institution in 1956 of the Children's Health Program and its extension in 1958 now provides for the child population of Newfoundland a complete range of medical services in hospital at public expense.

This recital of the successive steps by which Canadians have provided themselves with health insurance indicates clearly that the interest of government is no new thing and that the profession itself has taken the lead in demonstrating that personal medical services may be budgeted for by prepayment. In a series of policy statements the Association has undertaken to reflect the composite attitude of the Divisions, and the representative machinery of our organization has made possible the co-ordination of a diversity of views often in the form of the highest common factor of agreement. However, the Canadian Medical Association and its committees felt it necessary, and very desirable for their guidance, to test the reaction of doctors individually to the events and trends which have been summarized. Accordingly, after careful preparation and testing, a Questionnaire on Health Insurance was circulated to every Canadian doctor in the spring of 1960. The response was prompt and adequate and it has provided the Association and its Divisions with valuable information on the views, the desires and the preferences of that mythical figure, the Canadian doctor.

Whether political policy leads or follows popular opinion is an interesting matter for debate, but it was inevitable that the unmistakable interest of governments and parties in the provision of medical services insurance should find expression in a test of the electorate.

Health insurance was the central issue of the election campaign in Saskatchewan, which, in June 1960, resulted in the return of the party which had proposed this measure. It is possible that the outcome will focus the attention of other political parties on a publicly financed medical plan as an appealing objective to be promoted. The Saskatchewan Division is currently compiling its submission to the Advisory Planning Committee on Medical Care, using as its guide the Statement on Medical Services Insurance so painstakingly hammered out by the General Council at the Ninety-third Annual Meeting.

As this issue goes to press, the Prime Minister has announced his intention of appointing a Royal Commission "to study the health needs and re-

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sources of Canada with a view to recommending methods of ensuring the highest standard of health care for all Canadians". In the House of Commons, he said that this decision had been reached principally because of the recommendation of the Canadian Medical Association that such a study be undertaken. The significance of this step, taken after careful deliberation, will be regarded fifty years hence as marking the beginning of an era which, for good or ill, will profoundly affect the development of medical services in this country.

In this appraisal of the Canadian Medical Association during the period 1911-1961, it has been necessary to be selective rather than discursive. I have arbitrarily chosen to trace the steps by which the Association has transformed itself from a loose agglomeration of dedicated individuals to a representative and democratic national body which undertakes to co-ordinate our diversities into the semblance of a Canadian outlook. To illustrate the functioning of a national organization of doctors, the history of health insurance in Canada has been sketched. This represents in the sphere of organization an evolution as profound as that which has taken place in medical science. The end of the process is not yet evident. Difficulties and problems lie ahead, but it is not beyond the resources of Canadian doctors to preserve under any system of medical care those elements of current practice which are worthy and to continue to provide medical services of the highest quality to our fellow citizens.

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## FIFTY YEARS OF JOURNAL BUSINESS

T. C. ROUTLEY, M.D., F.R.C.P. [C], *Toronto*

HAVING HAD some contact with the business side of the *Canadian Medical Association Journal* for more than forty years, I would like to make a few observations, in this Golden Jubilee commemorative number, about the development and growth of the publication; the financial vicissitudes through which it has passed; the manifestation of faith in what looked to some like a sinking ship—in short, how the Journal has weathered fifty years of publication without missing a single issue.

As has been pointed out by MacDermot in his splendid history of the Canadian Medical Association, the Journal was launched on January 1, 1911, as an amalgamation of the *Montreal Medical Journal* and the *Maritime Medical News*. Incidentally, it began as the *Canadian Medical Journal*, and two issues had appeared before the word "Association" was injected into the title. How this came about is not clear from the records, but it probably stemmed from a desire to help the Association to become well known and to be truly national in character. This was a challenge to all doctors in Canada, calling for national co-operation.

Three parties were identified with the new journal: the Canadian Medical Association, which undertook to provide the contents; George Morang and Company in Toronto, who were appointed to act as publishers, to sell the advertising, pay the printer and retain anything which might be left over; and the Murray Printing Company, also in Toronto, who were engaged to do the printing. In addition, the Association agreed to give Morang a certain percentage of the subscriptions, which were then set at three dollars a year. The Association also undertook to give a rebate of fifty cents a year to each subscriber's local medical society. Clearly, the Association did not regard the new venture as a money-maker, as indeed it was not.

Before the Journal was 18 months old, Morang had fallen behind considerably in meeting the printer's costs. On March 1, 1912, he assigned to the Murray Printing Company, for unpaid debts, his interest in the sum of $1845.31, which was owing from advertisers. On February 7, 1913, he made a further assignment of $2162.49. Although at this point the situation looked precarious, Murray's agreed with the Association to continue publication until July 1913, and added to the document the three very significant words "if not longer". Thus, on June 6, 1913, Murray's became the publishers in place of Morang and Company, who do not appear in the picture again, and the words "if not longer" stretched over a very lean eight years. In August 1914, World War I began. During the next four years, hundreds, possibly thousands, of Canadian doctors, including the editor of the Journal, enlisted for military service.

Subscriptions, which had never exceeded 1200, fell off sharply and editorial assistance was depleted, but thanks to the efforts of a few volunteers and a well-disposed printing firm, the Journal never missed an issue throughout this trying period.

The years 1919 and 1920 will be remembered, particularly by the older generation of doctors, as a period of home-coming, readjustment and rehabilitation. However, during the war, a great many doctors from all sections of Canada became acquainted with one another in military service and undoubtedly this factor helped considerably in stimulating efforts to organize the medical profession nationally. One might say that Macphail's dream of a strong, united profession at last showed signs of taking root across the Dominion. Had this not been so, one can only speculate as to what might have been the outcome of a resolution, proposed at the Halifax meeting in 1921, that the Canadian Medical Association should disband.

At that time the Association had somewhat less than a thousand members, no assets, and debts of approximately $14,000. Thus the war and its aftermath had dealt the C.M.A. a hard blow.

But the pessimistic, defeatist resolution, after lying on the table overnight, was withdrawn the next day and replaced by a new one, the import of which was:

1. That the Association double its annual fee from five to ten dollars.
2. That a bond issue in the sum of $20,000 be launched among the members to wipe out all indebtedness and make provision for a fresh start.
3. That every effort be made to stimulate membership across Canada.

With enthusiasm, the meeting adopted the new resolution, the bond issue was quickly subscribed, and steps were taken to promote organization on a national scale.

With money in hand, we approached our largest creditor, the Murray Printing Company, in the late summer of 1921. In consultation with Mr. Douglas Murray, President of the company, the conversation went something like this.

"Mr. Murray, your company has been very considerate for the past several years as you have watched the unpaid account of the Canadian Medical Association grow to between ten and eleven thousand dollars. Why have you never pressed for payment?"

"Because we knew how the war and its aftermath had adversely affected the Journal. But we never doubted the good faith of the Association, and felt that one day it would get back on its feet and our account would be paid."

May I say that it was with considerable satisfaction that I handed over to the Murray Printing Company a cheque in full payment of their long overdue account.

Whenever reference is made to Journal publication, I hope the debt of gratitude which the Association owes to our printers, The Murray Printing Company, will always be remembered. How different the picture might have been had they been harsh creditors! They have served us for the past fifty years, both in lean and better times, with consideration and efficiency of the highest order.

And further, I would like to add a personal note; on that day, forty years ago, there began not only a business relationship but a friendship with Douglas and Joseph Murray which I have always valued. They both have passed on, but they have left behind a tradition which, I believe, motivates their successors.

With accounts all squared up, it remained for the Association and the printers to complete a new deal wherein the actual cost of printing was reduced, and the Association assumed full responsibility for production, including editorial and advertising copy. Murray's made it clear that they wished to continue as printers only; they were not interested in the Morang assignment beyond its relation to printing costs. This arrangement was completely satisfactory to the Association, which thus assumed full control of its Journal. Murray's returned all assignment papers to the Association and on August 10, 1928, the *Canadian Medical Association Journal* was copyrighted in Canada, thus completing ownership for all time.

Beginning in 1919 another interesting development took place in medical journalism which is significant in this narrative. In that year, the Macmillan Publishing Company of Canada founded the *Canadian Medical Quarterly*, which became the *Canadian Medical Monthly* a year later. In 1920 the Ontario Medical Association was undergoing active reorganization and felt the need of an official medical journal. Negotiations between Macmillan's and the Ontario Medical Association were begun and were about to be completed when the Canadian Medical Association entered the discussion. Chronologically these are the facts: In May 1920, the Macmillan Company advised the Ontario Medical Association that they were prepared to enter into a contract whereby the *Canadian Medical Monthly* would become the official organ of the Association, under the following conditions:

1. The O.M.A. to control all copy, text, and advertising, under the direction of an editorial board, to be appointed by the O.M.A.
2. The O.M.A. to receive one dollar per year per paid subscriber resident in Ontario.
3. All financial obligations to be borne by the Macmillan Company.

This proposal was accepted at the O.M.A. annual meeting in 1920 and a strong editorial board was appointed.

On October 1, 1920, my senior colleague, Dr. John Scane of Montreal, General Secretary of the Canadian Medical Association, approached the Ontario Medical Association and expressed the hope that the two associations would find it convenient to have but one journal and thus co-operate in making it a very strong one.

Macmillan's were then approached and, to the credit of that estimable publishing house, they agreed to sell the *Canadian Medical Monthly* to the Canadian Medical Association for $1200, although their promotional costs in developing the journal must have amounted to thousands of dollars. The deal was closed on February 11, 1921, thus incorporating a third publication into the *C.M.A Journal* and with it, an undertaking from the largest provincial medical association in Canada to assist the parent body materially in building not only a strong journal but a strong national medical association.

Commenting upon the consummation of this arrangement between the two associations, the editor had the following comments to make in the foreword to the January issue of 1921:

"The Ontario Medical Association has been especially prominent in its co-operation to bring

about the present change. The whole power of their provincial organization has been devoted to the success of one national Canadian journal. Their strong and well-organized editorial board has united to aid the scheme, and afforded an example worthy of emulation by the whole Dominion. The other provinces have already intimated their desire to co-operate; sub-editorial boards have been formed so that provincial interest may be served, as well as that of the country at large."

Accordingly, during the past forty years, the Journal has been proud to say that it is the official organ of the Canadian Medical Association and of all the provincial medical associations. It was clearly understood that each provincial medical association might, if so desired, issue a bulletin or periodical of a provincial nature, as indeed most of them have done.

The question has been asked frequently why the C.M.A. and the O.M.A. were so slow in getting together to promote one journal. I think the answer is provided by the fact that both associations were undergoing growing pains and were preoccupied with accelerating organization at the same time. Their nerve centres were several hundred miles apart, which at the time did not foster close co-operation. However, wise heads in both Associations got together just in time to make the arrangements which have been described, arrangements which, without doubt, have contributed greatly to the enlargement of the Journal and the strengthening and development of medical organization throughout Canada.

With this reorganization in 1921, the enlargement of the Journal and the elimination of the fifty cent per member rebate to the societies, it was hoped that the Journal would pay its way. That it failed to do so, for most of the next 30 years, can be regarded in retrospect as a compliment to the Association, which was more concerned with producing a good journal than in making a profit.

However, it was felt in 1950 that losses could be converted into gains by advancing advertising rates and introducing some business changes without in any way weakening the content of the Journal. Results have been gratifying, as during the past 10 years the Journal has not only paid its way but has produced considerable surplus revenue which has assisted the Association greatly in carrying on its constantly expanding services to its members.

In 1955 the monthly journal was converted into a semi-monthly. This was a bold step as it involved an increased budget from which the Association set aside a considerable sum of money to offset any initial losses which might be sustained. Fortunately, the new Journal carried itself from the beginning without any encroachment on the guaranteed fund and was so successful that on January 1, 1960, the next and final, logical step was taken by converting it into a weekly publication. It has more than paid its way in its first year as a weekly.

As the Journal begins its second half-century, there is every reason to believe that it will grow from strength to strength and continue to be a source of considerable helpfulness to the Association both in the dissemination of information and the provision of revenue.

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## CLINICAL CHEMISTS SALUTE THE JOURNAL*

E. H. BENSLEY, M.D.,† *Montreal*

THE FOLLOWING resolution was adopted unanimously by the Canadian Society for Clinical Chemistry at its Fourth Annual Meeting held during August 1960 in Montreal:

WHEREAS the first issue of *The Canadian Medical Association Journal* appeared on January the first, 1911, and the Journal will therefore celebrate its fiftieth anniversary in January 1961,

WHEREAS the Canadian Society for Clinical Chemistry is fully aware of the outstanding service rendered to medicine by *The Canadian Medical Association Journal* during its fifty years of existence,

WHEREAS the Canadian Society for Clinical Chemistry recognizes especially the contribution made to clinical chemistry by *The Canadian Medical Association Journal* through publication of communications in this field, and

WHEREAS so many members of the Canadian Society for Clinical Chemistry recall with gratitude the encouragement and help they have received from the Editorial Staff of the Journal,

BE IT RESOLVED that the Canadian Society for Clinical Chemistry convey to *The Canadian Medical Association Journal* heart-felt appreciation of the work of the Journal over the past fifty years, congratulations on its fiftieth anniversary, and best wishes and assurances of loyal support for the future.

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*From the Canadian Society for Clinical Chemistry and the Montreal General Hospital.
†Chairman of the Organizational Committee (1956-57), President (1957-58), and Member of Council (1957-60), Canadian Society for Clinical Chemistry.

The Society has given me the privilege of transmitting this resolution to the Journal. This I do with pleasure and, at the same time, I wish to use the opportunity to make a few personal comments about the Journal in relation to clinical chemistry.

Since my comments are personal, it is natural that I should start with a reference to my own laboratory, the Department of Metabolism of the Montreal General Hospital. The first papers to come from this laboratory were published forty years ago in the *Canadian Medical Association Journal*. Their author was my immediate predecessor as Director, Dr. I. M. Rabinowitch. They bore the following titles: "The prognostic value of the study of the blood chemistry in the acute abdomen",[1] "The prognostic value of the study of the blood creatinine in nephritis"[2] and "A simple method for determining the approximate degree of acidosis in diabetes mellitus".[3] The titles clearly show that these were contributions to clinical chemistry. Since then many papers from our Department of Metabolism have appeared in the Journal, and the growth of our laboratory can be traced in its pages. I am sure that on such an occasion as this I need not apologize for referring to my own department. However, lest it be thought that I give undue prominence to one laboratory and one hospital, I gladly record that the volume containing Dr. Rabinowitch's earliest papers also had two valuable papers bearing on clinical chemistry from our sister institution in Montreal, the Royal Victoria Hospital.[4, 5]

More than the story of individual laboratories can be found in the pages of the Journal. Much of the story of the development of clinical chemistry as a discipline and as a useful tool is also there. Modern clinical chemistry, based as it is largely on analyses of blood, was born at about the same time as the Journal, and the two have grown up together. I do not propose to attempt a dissertation on the history of clinical chemistry; my time for that is not yet. I can prove my point briefly and simply by comparing the contents of the fourth and fifth editions of Hawk's "Practical Physiological Chemistry". The fourth edition of this book,[6] published in 1912, contained no descriptions of quantitative chemical methods applicable to blood apart from the estimation of hemoglobin. The fifth edition,[7] published in 1916, contained a lengthy chapter on blood analysis setting forth methods for blood non-protein nitrogen, urea, uric acid, creatinine, creatine, sugar, acetone bodies, cholesterol, chloride, pH and fat. All these techniques required but small amounts of blood and yet gave reasonably accurate results. Thus when practical methods of chemical analysis became generally available, the Journal had just been launched. The Journal had an excellent opportunity to further the development of clinical chemistry and, under wise editorial guidance, it made good use of that opportunity.

Since chemical techniques, applicable to small amounts of blood, did not become generally available until between 1912 and 1916, it is not surprising to find that the first volume of the Journal, published in 1911, had no papers on clinical chemistry. However, it did contain a prophecy directly relevant to my theme. The prophecy was made by J. B. Leathes, Professor of Pathological Chemistry at the University of Toronto, in an Inaugural Address delivered before the Faculty of Medicine of that university on October 3, 1911, and subsequently published in the Journal.[8] Dr. Leathes spoke of his views of the importance to medicine of an understanding of chemical changes in disease and then he added, "But, you may say, granted that this is a scientifically interesting conception, it is certainly very abstract, very remote from the practice of medicine! But what is abstract to one generation may be a well-worn implement in the mental equipment of the next." Clinical chemistry has indeed become a well-worn implement during the past fifty years and in making it so the *Canadian Medical Association Journal* has played a significant role.

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## A HOSPITAL FOR INEBRIATES

(Reprinted from the *Canadian Medical Association Journal*, 1: 765, 1911)

A work deserving of the support of the public is that of the Ontario Society for the Reformation of Inebriates. It is now five years since the society was organized, and the work it is attempting is directly in line with that humane and wise view that characterizes present methods of dealing with the class which drifts into the police court.

The objects of the society, briefly, are: (1) To promote the reformation of indigent inebriates in Ontario, (a) by making use of the public hospitals of the province for the purpose, and (b) by combining therewith the Massachusetts probation system. (2) To promote the reformation of inebriates in Toronto as follows: A medical officer and a probation officer attend the police court, and offer medical treatment and help to inebriate prisoners. The medical treatment is given by the medical officer, either in the home of the prisoner, at the office of the physician, or in a ward of one of the public hospitals of the city. The probation officer acts the part of a friendly visitor, assists in finding employment when necessary, and helps in other ways.

The society is in need of a special hospital, entirely devoted to the treatment of inebriates. It is only in such an institution that these cases can be properly cared for and treated with any hope of success.

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# SPECIAL ARTICLES

## SCIENCE AND MEDICINE IN RUSSIA*

R. F. FARQUHARSON, M.B.E., M.B., F.R.C.P., F.R.C.P.[C],† *Toronto*

TO APPRECIATE the role of science and medicine, or anything else, in a rapidly changing country one should try to look at it from the point of view of its historical background. Towards this end I should like to make a few quotations about Russia from two famous nineteenth century authors; then give a brief outline of the history of the Soviet Academy of Sciences, largely as described by Vucinich[1] in a book published in 1956; and finally describe some of my own observations, modified by discussion with others, that were made during a trip to Russia in the fall of 1959 as a member of a group led by Dr. E. W. R. Steacie, President of our National Research Council, to arrange for an interchange of Russian and Canadian scientists.

On the last page of the first volume of "Democracy in America", published in Paris in 1835, de Tocqueville[2] makes the following remarkable comment and prediction about Russia and the United States:

"There are at the present time two great nations in the world which started from different points, but seem to tend towards the same end. I allude to the Russians and the Americans. . . .

"All other nations seem to have reached their natural limits, and they have only to maintain their power; but these are still in the act of growth. . . . The American struggles against the obstacles that nature opposes to him; the adversaries of the Russians are men. The former combats the wilderness and savage life; the latter civilization with all its arms. The conquests of the Americans are therefore gained by the ploughshare; those of the Russians by the sword. The Anglo-American relies upon personal interest to accomplish his ends and gives free scope to the unguided strength and common sense of the people; the Russian centres all the authority of society in a single arm. The principal instrument of the former is freedom; of the latter, servitude. Their starting point and their courses are not the same; yet each of them seems marked out by the will of Heaven to sway the destinies of half the globe."

Comparable striking predictions were made by Tolstoy[3] over a period of more than 30 years:

In 1865 he stated that: "The Russian revolution will not be against the Tsar and despotism, but against landed property. . . . The Autocracy will not prevent but will facilitate this order of things."

Again in 1881: "An economic revolution not only may come, but must come. It is extraordinary that it has not come already."

In 1893, pointing out that revolution was not the way out of Russian difficulties, he declared that "thanks to the efforts of communists and socialists" the new government would extend its control over the domestic and economic spheres "so that labour and recreation, housing, dress and food will all . . . gradually be prescribed and allotted by the governments."

In 1905, criticizing the Marxian socialists he said that their conception of revolution was change by violence; and that hence their leaders would be content to seize power, which they would retain by force and thus revert to the very oppression of the masses that they had set out to destroy.

Russia is moving actively in its historic role. The tremendous drive for extension of its power and influence still goes on. Tolstoy's predictions have been realized. The Soviet revolution did lead to the extension of autocratic control into new spheres which have included the Academy of Sciences. There are signs, however, that the type of control is being modified and that greater wealth is having its influence, perhaps not all for good, in Russia as in other countries. One would hope that the development of science and medicine may play a part in liberalizing this huge and powerful political machine.

### THE ACADEMY OF SCIENCES, U.S.S.R.

The Imperial Academy of Sciences was founded in 1725[1] by Peter the Great, the first academicians being imported from Western Europe. Beginning with emphasis on the physical and mathematical sciences, its scope was increased in the mid nineteenth century to include departments of Russian language and literature, and of political science and philology; to this day it is responsible for supreme direction of this broad field of investigation. With some setbacks science flourished in Russia; many famous Russian scientists were developed; the Russian scholars communicated freely with those in the West. The Academy was governed by a general assembly of academicians, leaving it great freedom of action to pursue investigation as it saw fit. In the summer of 1917 it had a staff of 45 regular members and 200 scientific and technical associates.

Before the revolution the intellectuals and socialists had been urging extension of scientific effort as part of a plan to improve the condition of the people. Just as the French Revolution was a great stimulus to science in France,[6] so in Russia the Soviet revolution led to a great increase in scientific

*The Fifth Annual Medical Alumni Oration, University of Toronto, October 13, 1960.
(Published in the Fall issue of *The Medical Graduate* by the Medical Alumni Association, University of Toronto.)

†Chairman, the Medical Research Council of Canada, and Emeritus Professor of Medicine, University of Toronto.

interest and activity. A new element was introduced, however, for Lenin was quick to recognize that the Academy might be made to aid in the building up and consolidation of the new Soviet society. He assigned it the duty of organizing committees of specialists to draw up plans for the organization of industry, the extension of electrification and the consolidation of small enterprises into huge industries on Western lines.

During the first 10 years the work of the scientists was little affected by these new demands. Under a new statute of 1927, however, the Academy of Sciences was transformed "into a typically Soviet organization". There was superimposed on its general assembly a presidium which was more open to external influence. Furthermore, secretaries were appointed in all its branches with a permanent and powerful senior post of Secretary of the Academy of Sciences, and all these leading administrative secretarial positions were soon held by communist academicians. The Academy of Sciences could now be used to further communist ideas as well as engage in research. It thus gradually became a state agency subject to communist inspection and control.

Relatively enormous funds were made available for building and equipping laboratories, and able young people were selected for training as scientists. Large numbers of specialized institutes were developed, and great emphasis was placed on applied science, while fundamental studies were discouraged. By October 1927, the scientific staff of the various divisions of the academy had increased to almost 1000 persons, and by 1941, when Russia became involved in the war, there was a staff of 10,000 persons. By 1949 it had risen to over 20,000, of whom over 6000 were classed as scientists. It still increases rapidly. "Today," as pointed out by Vucinich, "it is a gigantic enterprise, one which has no equal in the world in the scope of its scientific work, the versatility of its social functions, and the size of its staff." The Soviet Union has been true to its early policy of developing science rapidly, and at the same time trying to Sovietize it.

Had the increased support of science led only to concentrated effort along specified practical lines, the rapid development of technology and its application to industry would have been regarded as a wonderful effort. The deleterious effects of emphasis on applied research only might not have become apparent for a long time. But the Bolshevization of the Academy had other far-reaching, serious results besides the discouragement of pure research. One was a purge of noncommunist members in 1929 at the beginning of the first five-year plan. After violent personal attacks, many scientists disappeared, some never to be heard of again, others to be reinstated later. A second purge in 1936-38 was part of Stalin's great purge of the party in Russia, and affected only party members. It led to a general replacement of the secretariat with Stalinist communists, and a tightening of communist control. Scientists came more and more under party criticism. The submission of their plans to the hierarchy became an oppressive burden, and there was often disturbing, unenlightened interference both with the planning and execution of their work.

During the war when the Russians were our allies, these restrictions were greatly relaxed. It is interesting to read Kapitsa's report of his Institute of Physical Problems, written in 1943.[4] After describing his own successful work, he went on to make many critical and constructive comments which reveal the influence of his 15 years at Cambridge. He dwelt on the need for an institute to be occupied primarily with great (i.e. fundamental) science, while at the same time being willing to help in the development of practical applications. Scientists should spend most of their time in laboratories, he said, and only a limited part in social obligations and other functions. "One cannot do good work with other people's hands." A scientist should not occupy himself with several projects at the same time, particularly when beginning his career. He should have time to think about his work, read, study and rest. He deplored the downgrading of the university teachers to the level of pedagogues who do little research. Such teachers fail to develop the creative instincts of youth. There should be closer connections between the universities and the institutes. He emphasized also the need for communication, not only between different institutes, but also with scientists in other countries, remarking that "personal communication is the strongest communication". His report, presented at a meeting of scientists, won great commendation from a number of those present, many of whom, like Kapitsa, came under disgrace when Stalin tightened the fetters on scientific thought in the post-war period.

Distinguished scholars who then ventured to deviate from the party line, in history and economics particularly, where the party line must be followed closely, but also in biology and physiology, were attacked, as were also Kapitsa and a number of others who recognized the great advances made by western science. The common method of curbing non-conformism was through violent verbal and published attacks made by the victim's colleagues under the sponsorship of the party. Those attacked were expected to admit their mistakes publicly and fall in line. Should they fail to do so, they lost their administrative posts and much of their relatively large income, and were silenced.

The social sciences suffered tremendously from these curbs, but the physical scientists found means of studying fundamental and theoretical problems in spite of all the restrictions, and technology continued to thrive.

Dealing with the situation of the late Stalinist period, Vucinich remarks that "the Academy has become the highest scientific body in the U.S.S.R.

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in all respects but one: it deals with all the branches of systematized knowledge on a large scale, perhaps the largest in human history, and it is given exorbitant financial support, yet it has been deprived of the most cherished attribute of modern science—the right to pass judgment on scientific validity and to explore freely the unknown, the mysterious, and the unplanned." In spite of all this, he says, "the damaging effects of officially defined and policed scientific morality are considerably mitigated by an overall positive attitude towards science. . . . *In the Soviet Union science is held to be limitless in culture and power. For this reason, great emphasis is placed on the development of research facilities and the training of new ranks of scientists.* Popularization of positive scientific achievements, though frequently obscured by an adroit weaving of official myths into popular knowledge, has reached unprecedented proportions. Soviet natural scientists, despite the ominous checks imposed on them by communist guardianship, have done impressive work in almost every field of natural science. Many of their contributions have been recognized by the Western scholar. Soviet science is one of the most formidable tools in the hands of Communist dictators."

When, after Stalin's death, these curbs were eased, science in Russia seemed ready to move ahead rapidly and with safety. Many of those who had been silenced, like Kapitsa, came back to positions of influence and prestige. Stalin worship was declared alien to Marxism and Leninism, and public attacks on individual academicians ceased. It became established policy to have freer communication with Western scientists. Fundamental studies were encouraged. Soviet physiology and biology were eased of the major obstacles to free study. There has even been some easing of the curbs in the social sciences. The machinery for imposition of severe restrictions still exists, but the air is freer.

One fears, however, that the Russians do not yet realize that, as pointed out by Ashby,[6] "You cannot issue directives for scholarship and you cannot devise assembly lines for research. Orthodoxy, conformity, the party line, are all out of place in the scientific world."

## Our Reception in Russia

When our National Research Council group visited Russia in October 1959, we were received with great friendliness. There was unhampered discussion on scientific matters in all the laboratories visited. We did not discuss politics. The scientists indicated that they were free in the initiation and planning of their work, and it was pointed out that while ideas for study may come from the state or from the Academy, they usually originate with research workers themselves, whose plans as submitted are generally approved, and facilities and funds provided for the work.

The day after our arrival we were received by the presidium of the Academy of Sciences in its handsome, fine ancient building, said to have been given by Catherine the Great to one of her favourites. In one corner of the Board Room was a striking bust of Lenin carved out of wood. Pictures of former presidents of the Academy hung on the walls with, as everywhere else in Russia, portraits of Lenin.

The Russian scientists were most courteous. Arrangements were made for each of us to visit whatever institutes or laboratories he wished. All were taken to the Institute of Scientific and Technical Information, and to the high energy accelerator at Dubna, situated on the Volga, in surroundings similar to those of our Chalk River plant on the Ottawa River. Arrangements were also made for us to see places of interest as we went along. We visited the Kremlin, the exhibition of Soviet achievement in Moscow, the summer palace and the Hermitage in Leningrad; art galleries, the ballet, concerts and universities in all centres. Everywhere we found interest and veneration for former great Russian czars and for old Russian architecture, art and literature.

## Russian Interest in Foreign Publications

Russian interest in foreign publications is demonstrated by the great development of their Institute of Scientific and Technical Information, which was organized by the Academy of Sciences and the Scientific Commission of the Council of Ministers in 1952. It occupies a many-storied building where foreign journals are abstracted by 1800 scientists, who are aided by some 17,000 extramural part-time abstracters in centres across the country. I visited the medical section and saw Canadian and other journals with which we are familiar, and many more including trade journals, all being abstracted into Russian. When I asked the physician in charge if he did not become bored with the work of abstracting, he admitted that it might be boring in certain respects, that it lacked the daily changing interest of clinical work, but added that there was great satisfaction in getting good abstracts into print quickly. This was the spirit of the place. In the Institute they receive about 50,000 publications per year, journals, books, transactions, reports, of one kind or another, of which about 12,000 are suitable for abstracting. After receipt of a journal in Russia, an abstract is published in Russian in pamphlet form in 30-40 days, and in larger journals in 4-10 months. On request, a photostatic copy of the full article will be sent to any scientist or technician. It is interesting that one of the scientists in the Institute said in casual conversation, "English has become the language of science; all scientists must learn English." In Russia, English is taught in the high schools.

### QUALITY OF RUSSIAN SCIENCE

For two centuries Russia has always had its great scientists, particularly in the field of mathematics and physics. Russians appear also to have a natural aptitude for engineering and have made wonderful strides in electronic technology. All their efforts have been expanded since the revolution, and while greatest attention has been paid to the development of technology and its application to industry as well as to sputniks, the advance is along the whole front of science. Perhaps, as C. P. Snow pointed out,[5] the Russians understand better than do the Western powers the driving force of the scientific revolution which has been accelerating for two centuries or more. They may be adapting better to its inevitable changes by selecting more of their brightest young people and giving more freely of their resources for the active pursuit of research and technology in all fields. Nevertheless, in the broad field of science they are still behind the Western world.

### MEDICINE

In a book published in 1912, MacKenzie Wallace described his experiences in Russia, beginning in the 1870's. Taken ill on the estate of a friend who was a Russian nobleman, he was surprised to find that there were no doctors in the neighbourhood, but only feldshers, old soldiers who dress wounds and give physic. The feldsher who came to see him proved to be quite an intelligent, kindly old man who had learned much about people by years of experience. He commented intelligently on outbreaks of cholera, plague and smallpox, which occur especially in hot summer weather when there are numerous barges passing along the Volga. In conversation with Wallace he made the astute observation that after people came to know and trust him everything he gave them seemed to do them good, even when he did not understand what their trouble was. "I believe," he said, "that faith does as much good as physic."

After the revolution, great emphasis on public health soon made it a safer country to live in. The rapid training of all grades of medical personnel—doctors, nurses and technicians—along Western lines soon led to great improvement in all branches of medicine, and this is continuing.

In an article in the *Moscow News*, a propaganda sheet published for visitors, in English, which I purchased in Moscow on Wednesday, October 14, 1959, Alexander Bakulev, President of the Academy of Medical Sciences, described medical activity and progress in Russia. Medical research, he pointed out, is conducted in institutes supported by the Academy of Medical Sciences or by the Department of Health, and is concerned primarily with questions of interest in practical medicine. There are over 300 medical research institutes. All are being expanded rapidly. Quite without embarrassment he speaks of the headway they have made, having wiped out smallpox, plague, cholera, ringworm and recurrent typhus. In a seven-year plan it is expected that malaria, typhoid, dengue, diphtheria, trachoma, leishmaniasis, and a number of helminthiases will be largely eliminated. In a simple, if rather grandiose, statement he announces that Soviet biologists, armed with the latest methods of scientific investigation, have set themselves the task of discovering the physical and chemical aspects of the phenomena of life. They wish to penetrate into the secrets of metabolism and biosynthesis, growth and propagation, heredity, excitability and response reactions. He went on to talk of electronics in medicine, the use of electron microscopes, the development of memory machines which, after being fed information of symptoms and signs, give answers that allow a physician to make a diagnosis quickly and more accurately. He states that cancer will be cured, and speaks of production of experimental tumours by viruses and other methods and treatment by drugs, radiation and surgery. He talks of facing big tasks in the evolution of nation-wide measures for prevention of cardiovascular diseases, and of the use of surgical measures in treatment of heart diseases. All this, he says, has to do with the main principle of Soviet medicine—prevention of disease and extension of the life span.

It is interesting, however, that the President of the Academy of Medical Sciences, even confusing the past and present with the future, was unable to point to any notably great achievement in medical research. It would appear that no potent antibiotics and no highly valuable new drugs, such as Western pharmaceutical houses have produced in large numbers in recent decades, have been discovered in Russia. Their medicine has, however, copied Western medicine and while doing so they have advanced greatly in the Western image from their pre-revolutionary period. The hospitals that I saw, probably their best, resembled our hospitals. Their clinical records, written in Russian which, of course, I could not understand, seemed to follow our pattern. In their treatment record sheets, which like ours abounded in numerous entries which would confound any visitor trying to find out what treatment the patient was actually receiving, I could make out the words penicillin and streptomycin written in English. Their doctors in university hospitals and research institutes seemed to be interested, intelligent, and competent. I felt, as have other Western visitors with whom I talked, that their medicine definitely lags behind ours, but that it is catching up and that their medical research, escaping from the fanatical control of the Stalin period, conducted by many full-time intelligent workers in well-equipped but often not new laboratories, is constantly improving and likely to become great. It may continue to suffer from the heavy hand of too much central planning as well

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as from certain traditional influences, which include those related to the rigidity of the Soviet system, but the tendency is to escape from such controls as medical science develops.

### VISITS TO INSTITUTES

Medical research institutes are divided into those dealing with physiology, pharmacology, biochemistry and the like, which are supported by the Academy of Sciences, U.S.S.R., and the highly specialized clinical institutes supported by the Academy of Medical Sciences and the Department of Health. Both are separated from the universities and medical schools. This organization allows of concentration of great resources in one place, but leads also to the harmful effects of too much isolation and resultant narrowing of outlook.

In the large Moscow Institute of Higher Nervous Activity (i.e. neurophysiology), with its 90 scientists, investigations range from repetition of Pavlovian experiments to modern electrophysiological studies of special senses and, as in other experimental institutes, investigation of radiation injury and its repair. They asked why, in Canada, so little work was being done in neurophysiology, and why, in studying radiation injury, so little attention was paid to damage to the brain and spinal cord. In Russia, they said, we look at the central nervous system first.

The Institute of Neurosurgery, with its 350 beds, is located in a fine old building which was formerly an aristocrats' club. There were two narrow Russian beds in each room; the rooms opened on a wide corridor with numerous easy chairs for patients to lounge in. The staff included 17 clinicians for care of patients, and some 70 scientists studying in pathology and other fields. Up to 1958, Professor Egorov said, 24,800 intracranial operations had been performed, and 42% of these were for removal of brain tumours or palliation of their effects. Patients with brain tumours are referred from all over Russia, and this work dominates the institute.

In a similar but newer Institute of Chest Surgery, operations on the esophagus, lungs and heart are performed. They have modern wards and operating rooms, and modern well-equipped laboratories with profuse electronic equipment. Earlier in 1959 a surgical team from the British Postgraduate School at Hammersmith had come to train Russian surgeons in open heart surgery. I was told later in London that the Russians had been apt pupils.

The Institute of Surgical Instruments in Moscow is unique. It is the only one in Russia, and probably there is none like it elsewhere in the world. Here, over 200 engineers, physicians, surgeons and pathologists study the improvement and development of new surgical instruments, as well as of all types of apparatus and electronic and other equipment for clinical and laboratory work. On completion of a new design, the blueprints are given to manufacturers for production. Whether it is a good thing to concentrate a nation's efforts in the development of instruments and apparatus in one large active institute is open to question.

They have been particularly interested in the development of stapling machines for the rapid end-to-end suture of arteries and veins, for rapid stapling of the pedicle of the lung in lobectomy, and for use in gastrointestinal and other surgery. I have been told by visiting surgeons that these stapling instruments are not used in routine work. This might be due to lack of communication, a fairly common fault in Russia, or to the unsuitability of the instrument for ordinary work.

They do, however, use their new stapling instruments in experimental surgery in their own institution. They were particularly proud of their ability to reattach successfully the hind limb amputated from a dog 30 hours before, and kept after perfusion with saline in a refrigerator till warmed up again by perfusion just before reattachment. I saw one of these dogs running about with very little limp 18 months after the procedure. This type of work seems to appeal to them greatly. Russian workers, while claiming to be interested in practical applications, often pursue the abstruse and the bizarre.

In the Institute of Surgical Instruments, as in many others, the visitor is likely to be photographed again and again, especially when he is listening attentively to what is being told or demonstrated to him. I saw pictures of a number of American and British visitors on their walls. Like other visitors, I was also asked on repeated occasions to write in a visitor's book what I thought of the place and the work being done. One learned to think as he walked around of what he would write when the book was placed before him.

There was not time to visit the many other institutes in Moscow or other centres. It is likely that we were shown the ones of which they were most proud. In Leningrad I was much interested in seeing Pavlov's institute, part of the large 70-year-old Institute of Experimental Medical Sciences which has a total staff of some 200 scientists and 400 technical assistants. Similarly in Kiev we visited the Bogomolets Institute of Physiology, staffed by 120 scientists and 180 assistants. In all, one saw much repetitive Pavlovian work; a good deal of abstruse study; some workers who spoke boastfully of their achievements, and also many competent modest workers who had a good appreciation of world science and a wish to be part of it. One was struck by the emphasis on neurophysiology, and by the attention given to radiation injury and radiobiology.

### MEDICAL EDUCATION

There are 80 medical schools (medical institutes) in the U.S.S.R., and all are under the direction of Professor Starobinsky, a deputy minister of health

from whom I obtained most of the following information.

Except in smaller states, the medical and engineering schools are separate from the universities.

Medicine is an attractive profession in Russia, and only one of ten applicants can be accepted for enrolment. The requirements for admission are very like ours. The Russian high-school student is required to take a broad course of studies, and it is said that he is given an excellent training in physics and chemistry, as well as in broad cultural subjects, including mathematics. Selection is made on standing, some preference being given to nurses. Since the students are good to begin with, and since they work very hard to hold their place, there are very few failures during the medical course.

In all the large centres, medical institutes have five faculties, namely: General therapy (or general adult medicine), Pediatrics, Hygiene, Stomatology (Dentistry), and Pharmacy.

In the year 1959, some 25,000 students were graduated from the 80 medical schools in the U.S.S.R. Of these, 14,000 were in general medicine, 3000 in pediatrics, 3000 in hygiene, and the remaining 5000 in dentistry and pharmacy together*. One can easily see that the number of doctors being graduated in Russia each year is much greater than in the U.S.A., where the number of schools is about the same but the average number of graduates less than 100 per school. In earlier years, the proportion of women medical students ranged up to 70 or 80%; now men and women are about equal in numbers. I had been told that this is because medicine is being upgraded, a statement denied by senior officials.

The curriculum is the same in all the medical institutes in the U.S.S.R. The actual teaching, of course, will vary with the qualities of teaching staff. In general, the outline is much as in our own schools. The course consists of six years. The students attend six hours a day for six days a week. The first year is devoted to physics, chemistry and biology, with, of course, Marxism and Leninism. The student studies anatomy, physiology, biochemistry and microbiology in the second year. Pathology and pharmacology are important third-year subjects, but medicine, surgery, pediatrics and hygiene are begun then. In the fourth and fifth years students begin to specialize in their respective faculties. The general physicians spend most of their time with adult medicine, and relatively little in pediatrics and hygiene. In these two years they learn to take histories and examine patients, and study particularly medicine, surgery, obstetrics and gynecology. Those in pediatrics and hygiene spend their time in their respective fields. The hospital records are written largely by fifth- and sixth-year students. A start in this activity is made in the fourth year. The final-year students in medicine and pediatrics act as virtually the only "interns" in the hospitals; they take responsibility for the care of patients on a six-hour shift basis, but they do not live in. Those in hygiene spend their time in field work. There are no lectures in the final year.

During their course, medical students are paid, as are students in the universities and other teaching institutes. The rate varies from 300 roubles per month in the first year to 500 roubles per month in the fourth year, students standing in the upper ¼ to 1/3 of the class receiving an additional 25%. There are no fees. (In Russia the minimum wage for labour is 400 roubles per month, an ordinary artisan may receive 800-1200 roubles, and highly skilled electronic technicians, as much as 2200 roubles per month.) If a student has worked at other occupations for some time after graduating from high school, he continues to be paid the wage rate of his interim occupation.

On graduation, the young doctors are placed by the local ministers of health of their respective states, consideration being given more than formerly to their own choice of location. The great majority of them go directly into general practice. In 1959, only 600 of 20,000 graduating doctors were selected for immediate postgraduate training. Opportunities for advanced training are given later to many more, depending largely on performance.

The remuneration of a general practitioner is very small by our standards, being actually about the same as that of a teacher. To begin with, he receives 800 roubles per month and his maximum monthly rate, reached after 10 years or more, is 1500 roubles. The doctors and the teachers work only six hours per day, however, and may be able to augment their income by working an extra shift. Their hours are shorter than the hours of factory workers. When I remarked to a very intelligent young woman in Moscow that it seemed strange not to pay a doctor more than a bricklayer, she replied, "Wouldn't you sooner be a doctor? Why do you demand more pay for doing the work you like?" Engineers are, however, paid about 20% more than physicians, an indication of the importance attached to engineering in Russia.

On the other hand, those physicians who are selected for advanced training have their income increased on progression from step to step. On attainment of a doctorate, roughly equivalent to our Fellowship in the Royal College, the salary is increased at once to 2700 roubles. A professor receives 5000 roubles per month. Should he also be placed in charge of a clinic, he is given another 1000 roubles. For service on special commissions or boards, and the writing of papers, there is additional remuneration. Appointment to membership in an Academy of Science brings a big increase in income. The Russians believe in payment for further training, and for academic and scientific excellence.

*I have not exact figures for the numbers in dentistry and pharmacy. There has been a great shortage of pharmacists and their numbers are accordingly increased.

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### MEDICAL SERVICE

The general care of patients is managed in clinics, and each big organization, such as a large factory, or the Academy of Science, has its own clinic. Records are kept of all patients. When I questioned whether one could ask for his own doctor at the clinic, I was told that of course one could ask; in Russia one can always ask. But commonly one sees whoever is there at the moment. Patients are sent to hospitals or special institutes for consultations and special measures in diagnosis and treatment. One might add that house calls as we know them are uncommon. If a doctor must visit a patient in his home for an emergency illness, he goes in a state taxi. Doctors, like the great majority of people in Russia, do not have motor cars.

I visited one pharmacy near our hotel in Moscow. There was no pharmacist there, but one could be reached when necessary for consultation. Drugs were supplied in small packages of tablets, and the drugs I saw were sulfonamides, old-fashioned sedatives, antibiotics, great quantities of vitamins, and a number of drugs that are now out of fashion in the Western world.

It is evident that the Russians are proud of their medical service. They believe that it is excellent in all respects, that they have the best medical care in the world, and they tell with pride that it is available to all.

### GENERAL REMARKS

It is apparent that the Russians are proud of their country and of its history. They are Russians before they are communists, but communism has been a great instrument for the advancement of Russian nationalism.

They have been copying Western methods in everything but politics and, of course, Marxism and communism are Western importations. One sometimes wonders if those responsible for the rapid development of their country are not fascinated by the methods of capitalism. In any case the people wish to equal us, and they are anxious to have our approval and our admiration. The scientists and medical people, and all those we met, wished to be friends with us. All were polite and courteous.

There is no doubt of the tremendous interest of the Russian people in education and of their great belief in science. They study with earnestness and intensity from their early years. The earnestness of people in Moscow is almost unalloyed by any obvious sense of humour, which, on the other hand, is in greater evidence, with a feeling of relaxation, in Leningrad, Kiev and Tbilisi. All seemed to have pride in the great improvement in their standards of living since the revolution, and it is not surprising that they could hardly realize that there had also been similar great improvement in Western countries in that time. Pride in Russia and a desire to have peace seemed to be their dominant emotions.

* * *

The more one considers our world, the greater seems to be the importance of communications between the people living in countries that may be hostile to one another. Perhaps the easiest way to further it is by communication of scientists of all kinds. Our arrangement for exchange of scientists between Canada and Russia is already working well, and one hopes that multiplication of such communications in all countries may have a salutary effect. This theme is well developed by Sir Eric Ashby[6] in his book, "Technology and the Academies", where he states that "In an age bedevilled by nationalism universities have, through their adaptation to science, become the chief trustee for the only supra-national movement in the world. . . . In our generation the urge towards nationalism has increased until it has become a cancer destroying nations and leaving untold misery behind. Meanwhile there has appeared a new cement . . . a common way of thinking about nature, and a common stock of knowledge. Today . . . when scientists are reckoned not by their dozens but by their hundreds of thousands, this commonwealth of universities (and scientists) becomes one of our hopes for the sanity of the world."*

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*It is interesting that since this paper was written, the Hon. J. Waldo Monteith made the following comment at the end of an address to the Annual Meeting of the Ontario Division of the Canadian Cancer Society in Toronto on November 23, 1960: "Medical research holds an important key to the future welfare of Canadians. But it has another significance which Dr. Banting saw as early as 1926. Speaking to the Canadian Medical Association in Victoria, he made the following comment which to my mind is even more to the point today than it was at that time. He said: 'Medical research is the most truly international commodity we possess. It knows no protective tariff, no embargo, no boundary line to prevent its free dissemination for the good of all. It is the common language and common spirit among the nations.'"

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### ERRATUM

In the article by John R. Seeley, "Death by Liver Cirrhosis and the Price of Beverage Alcohol" (*Canad. M. A. J.*, 83: 1361, 1960), acknowledgment was inadvertently omitted to the effect that the author was indebted to Mr. Harold Greer and the Toronto *Globe and Mail* for the use of extensive data prepared by Mr. Greer for a series of articles published in the *Globe and Mail* and subsequently placed at the disposal of the author and the Alcoholism Research Foundation of Ontario. This indebtedness on the part of the author and the Foundation is hereby gratefully acknowledged.

# MEDICINE, LAW AND THE UNIVERSITY*

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IT IS NOW five years since law and medicine agreed to foregather in peace and amity and to have their graduating classes share that sweet sorrow of parting from the University of Toronto. It must be revealed that there were periods in our long history as professions when we had either no relation at all, or at best a very tenuous association with a university.

It is of interest to remember that training for both medicine and law preceded by many centuries the establishment of universities. Indeed the celebrated school of medicine at Salerno, where in the very early days of the Renaissance, Arab and Greek medicine were being revived in the 10th century, was the beginning of the first university. It is also fair to state that Bologna, another early university community, had been known for a century before the birth of the university idea, as a great training ground for both civil and canon law. The story of university development is relatively easy to follow for the next ten centuries—at Paris and other continental centres, and then the foundations of Oxford, Cambridge, Glasgow, St. Andrews and Edinburgh in Britain, Harvard and Virginia in the new world, with our own university being founded here in 1827, although it did not exercise its teaching function until 1843.

But law and medicine were often found following their own ways independent of universities between the 10th and the 19th centuries. In London, medicine developed in association with hospitals, the academic side being largely fostered by such organizations as the Royal College of Physicians and the Royal College of Surgeons. Indeed the association of medicine with the University of London is a relatively recent event. The Royal Colleges, which in effect were associations of practising doctors, were recognized as the authority for granting certificates for practising physicians long before the universities took any interest in such affairs. Likewise in law, the training of barristers and solicitors was centred in the Inns of Court, organizations of practising lawyers, and, as is well known, the lawyer even to this day in England still seeks his licence or call to the Bar by an association with one of the various Inns of Court in London.

This dissociation from universities, and indeed from any government authority which might safeguard the qualifications for practice, resulted in the so-called trade schools of medicine—organizations which taught by the lecture method the elementary principles of anatomy and pathology, and something of the then known outlines of treatment. The last of the trade schools in Glasgow closed its doors within recent years. In the United States, there were 180 schools of medicine in the early years of the present century, the majority of which were diploma mills or trade schools; these all disappeared after the Flexner report of 1910.

In Toronto, with the establishment of a university, provision was made for courses in both medicine and law. In 1845, there were 14 students enrolled in law and 13 in medicine. It is interesting to recall John Strachan's remarks about the need for lawyers when he was reviewing the state of higher education in Upper Canada. "Lawyers must from the very nature of political instructions, from there being no great landed proprietors or privileged orders, become the most powerful profession." What an admission from this great Scot who, having espoused the Church of England, worked so faithfully in advancing its interests in Upper Canada! Thirteen years after its establishment, teaching in law and medicine was discontinued. The Hincks Government of the day took the position that public funds should not be used to provide training for young men who were likely to improve their own financial position by achieving the status of practising lawyers or doctors. George Brown of the opposition party moved for a further consideration of the teaching of law and medicine by a committee of the whole, but his motion was defeated. It was to be 34 years before a professional school of medicine was re-established in the University of Toronto, and an even longer period before an organized course in law was offered.

Both law and medicine were regarded as beyond the sacred sanctuary of the temple of learning where men pursued the truth in study of the classics, literature and philosophy. Again to quote Strachan in relation to lawyers (a statement uttered in admiration): "They are emphatically our men of business and will gradually engross all the colonial offices of profit and honour." Something of this philosophy of Upper Canada has continued to pervade the educational thinking of our people through the century that has passed since the decisions of the Hincks Government. Primary and secondary education have enjoyed liberal support, and were early accepted as not only a desirable but a compulsory preparation for citizenship. Higher education, particularly if it related to preparation for professional practice, was something to be achieved only through parental or personal financial sacrifice, by work in the purposely-planned long summer vacations, or by winning the occasional scholarship.

To understand better the attitudes of governments, scholars and educational philosophers towards this divorcement of the professions from the more peaceful pursuits of the humanists, one may with profit go back some twenty-six centuries. Viscount Soulbury, in an excellent paper recently published in the *Canadian Medical Association*

*Address to Convocation for the Faculties of Law and Medicine, University of Toronto, June 10, 1960.

*Journal*, records some interesting comments on the history of science and the humanities. They have been at odds for more than two thousand years, and law, which in some strange way has frequently been regarded as a technique, has found itself classed with medicine and technology.

Modern medicine can trace its beginnings to the teaching of Hippocrates and his disciples between the years 600 B.C. and 400 B.C. In those days it was no sin to be practical, and the early scientists did not lose caste with the philosophers. "Careful observation, patient research, and experiment, not abstract speculation were the keys to the comprehension of nature." In the succeeding Socratic age, both Plato and Aristotle discounted the scientific method, and gave pre-eminence to logic and metaphysics. In the words of Soulbury: "It is to the immense influence of these two philosophers, and particularly Aristotle, on Western thought that we can ascribe much of the separation of technology from the humanities that has only commenced to disappear in recent times. Plato's metaphysical theory of reality implied that technique was less worthy of esteem than thought, and the status of the technician less reputable than the thinker." Aristotle, however, was prepared rather grudgingly to grant citizenship to a physician, perhaps remembering his own father who practised medicine. The legal philosopher was probably also recognized, but not if he became interested in law as applied to commerce. Industrial and commercial life involved sordid occupations, detrimental not only to health but to character. Aristotle was under the impression that material progress had come to an end, that there was no need for practical science.

Now after two thousand years, Sir Charles Snow, in his Reid Lecture, discusses the continuing separation of science and the humanities. The scientist fails to comprehend the world in which the old-fashioned philosopher lives and thinks, and the student of the humanities is lost when dealing with the leaders of the scientific revolution. Dr. Jacques Barzun says that the failure of communication is largely the fault of the scientist; that he has not as yet developed a language which adequately describes and is capable of communicating to the uninitiated the beauties, the emotional effects of the discipline, the world in which he lives.

Perhaps we have come full circle since the far-off days of Hippocrates and Thales when it was quite respectable to observe, experiment and apply one's knowledge for the benefit of man. Indeed, it was reported that Thales, having some knowledge of astronomy, was able to turn it to good effect, and to corner the market in olive oil against a year of drought and bad crops.

At any rate, most universities in the Commonwealth now accept both law and medicine as reasonable disciplines to be included in the institution which is so frequently, and quite properly, described as a community of scholars. It is generally accepted that a university should be soundly and firmly based on a Faculty of Arts, in which there are opportunities for scholarly effort in both the sciences and the humanities. There is, however, still evidence of the two-thousand-year-old conflict between the two great branches of scholarship. The honour student in English, history, philosophy or classics has little cause or desire even today to know something of the science which is virtually launching him willy-nilly into a new, unknown and uncertain world. If a study of the humanities means the study of man, both medicine and law should properly be included. In no other discipline has such an intensive effort been made as there has been in medicine of late years to understand man, his emotions, his shortcomings, his failures and his reactions to the world about him. Similarly, the lawyer is in a very special and preferred position to study man's behaviour, and the methods and rules by which men may live together in some measure of amity. Furthermore, legal training has been recognized as an eminently suitable preparation for service in the government of one's country. Even Aristotle would have granted that the study of governments and the exercise of democratic control of the citizenry might be efforts worthy of the humanist.

All of you have spent at least two years in the study of the so-called liberal arts. Many of you are already graduates in arts. But it is not by reason of that qualification alone that I can address you all as humanists, but as young men and women who have had a sound introduction to the study of man, and who will continue that study, and disdain not the various practical measures by which man may be aided in his age-old struggle to achieve some measure of health and happiness.

To the universities which have accepted us after nearly a thousand years of wandering in the wilderness, we are grateful for the clear beacon-light of scholarship which has served to remind us of our early Greek heritage, when law, medicine, and religion were pursuits that commanded the highest intellectual effort. We know that the universities may at times find us rather trying. Like older members of a family who have been away on their own and done fairly well by themselves, we may have developed expensive tastes and some desire for a reasonable measure of independence within the family circle. We may not conform too readily to educational philosophies and administrative techniques evolved primarily to suit undergraduate faculties of arts or even schools of graduate studies. Nevertheless we hope, and indeed have some reason to believe, that we have justified our admission to communities which in fact we had a part in founding. Although the results of our study, investigation and research may sometimes be reflected in practical improvements in the way men live, we shall nonetheless stoutly maintain our right to membership in a community of scholars.

It is inherent in both our professions that the basic undergraduate course should teach broad principles. It has also, one hopes, encouraged skill and integrity to use these principles in further learning. Truly for either the doctor or the lawyer there is no ultimate goal of education. The introduction of the case method in law and the clinical method in medicine has allowed for the combination of professional knowledge and experience with the greatest opportunity for seeking the fundamentals of scholarly knowledge. Whether you young lawyers may be wrestling in 1980 with the principles governing the rights of outer space, or of the rights of man and nations to the unknown harvests on the bottoms of the seas, I am confident that the principles you have been taught in the last three years will enable you to solve the most abstruse problems which may arise. To you who are leaving the medical school, it is equally true that we can only hope that the principles of medicine which you have learned in the laboratories and in the wards of the hospitals will enable you to deal with such equally new and unimagined problems as may present themselves in this brave new world.

Perhaps I can wish you nothing better than some measure of success in bridging the gap between the humanities and science. In the words of Hippocrates: "Where the love of mankind is, there also is the love of science."

# ORIGINAL ARTICLE

## RADIOACTIVE IODINE IN THE TREATMENT OF HYPERTHYROIDISM EXPERIENCE AT THE TORONTO GENERAL HOSPITAL, 1950-58*

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PART II‡

### POST-$I^{131}$ THYROIDITIS

ACTUAL CLINICAL thyroiditis with severe thyroidal pain was a rare occurrence in this series (three patients). Mild thyroid gland tenderness, not noted by the patient until elicited by the palpation of the examiner, was not uncommon in the patients given larger doses.

Apparent clinical exacerbations after radioactive iodine therapy were uncommon, although there was sometimes some subjective increase in symptoms in the 10 to 20 day interval after the dose. Thyroid crisis has been rarely reported in the literature.[26, 53-55, 106] In this series, two patients dying within one week of treatment were considered by their attending physicians to be suffering from thyroid storm (see "Deaths"); however, both had pneumonia and severe cardiovascular disease. In our view, neither patient was actually in thyroid storm, nor could their clinical state be ascribed to the $I^{131}$. These cases will be subsequently discussed.

It should be noted, however, that a few patients experienced increased angina pectoris, and some of the cardiovascular deaths later reviewed may possibly have been related in part to therapy.

### PERIARTHRITIS OF SHOULDER, AND "RHEUMATIC" PAINS

A small group of nine patients developed "periarthritis" of one or both shoulders after $I^{131}$ therapy. Muscular aches and pains were not uncommon, although severe muscular aching was generally the first harbinger of hypothyroidism.

### SIZE OF GOITRE

In virtually all of the diffuse goitres, as well as the post-thyroidectomy recurrent goitres, the goitre regressed to a normal or subnormal size. In the toxic nodular group there was invariably a reduction in size of the goitre, which occasionally was complete. More often, nodules persisted although the glands were much smaller in size, often not even of cosmetic consequence. No *new* thyroid nodules have been noted in the follow-up in this series. It is noteworthy that patients with tracheal compression were treated without complication.

### EXOPHTHALMOS

No exophthalmos was observed in the "toxic nodular" group. Since we did not perform routine exophthalmometry in most patients, we have no accurate data on the changes in the eyes in the

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The work was carried out with the technical assistance of Miss Norma Huber, R.N., R.T.(Can.) and William Paul, Ph.D.
†Medical Research Fellows, National Research Council, 1950-57.
‡This is the second of three instalments in which this paper is being published.

"toxic diffuse" group. Of 185 patients with exophthalmos, 25 (13.5%) showed definite improvement; 7 patients were transiently worse but later improved, and two were definitely and permanently worse following radioiodine treatment.

Sheline and Miller[34] have analyzed their exophthalmometric data, although these data were admittedly not complete. In 62% there was no change in eye measurements; in 24% there was an increase in exophthalmos of 2 mm. or more, and in 14% there was a decrease of 2 mm. or more. It was noted that this study compared favourably with a similar study by Soley[35] concerning exophthalmos after subtotal thyroidectomy. In assessing only patients with *moderate to severe* exophthalmos (44 cases), Chapman and Maloof found improvement after $I^{131}$ therapy in 23, no change in 17, and worsening in 4.

Exophthalmos *first* appeared after $I^{131}$ therapy in three patients in our series, but was not severe in any of these.

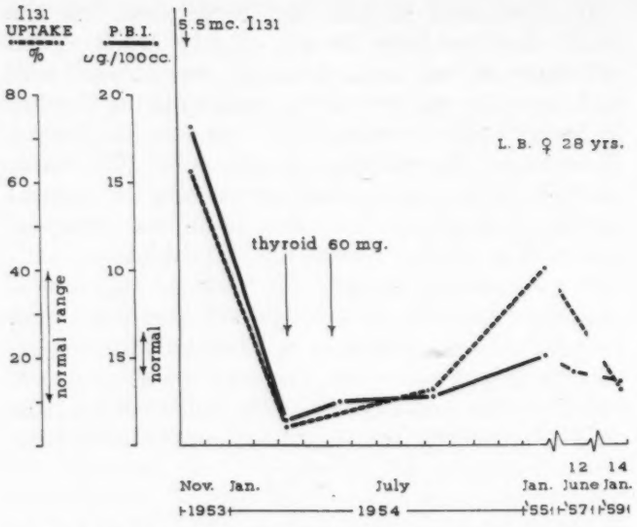


**Fig. 6.**—Transient hypothyroidism after $I^{131}$ therapy. Four months after a single dose of $I^{131}$, this patient developed clinical and laboratory evidence of hypothyroidism, necessitating thyroid therapy. Later she regained a euthyroid state spontaneously. Note the "rebound" of the $I^{131}$ uptake with recovery.

### REVERSION OF AURICULAR FIBRILLATION TO NORMAL CARDIAC RHYTHM

Auricular fibrillation was noted before therapy in 40 of the "toxic nodular" patients and in 61 of the "toxic diffuse" patients. In only 6 of the former and 17 of the latter group was there recorded reversion to sinus rhythm following treatment. This reversion occurred when a euthyroid state was reached. In the remainder, the abnormal rhythm persisted despite the regression of other abnormal cardiovascular signs. In those who remained in fibrillation, there was generally evidence of severe organic heart disease. Of 27 hyperthyroid patients who were fibrillating, Chapman and Maloof[1] found that after radioactive iodine therapy 12 reverted to sinus rhythm, 8 were euthyroid and still fibrillating, and 7 were still hyperthyroid and still fibrillating. Blomfield *et al.*[26] noted a return to sinus rhythm in 33 of 90 fibrillating hyperthyroid patients after $I^{131}$ therapy.

### HYPOTHYROIDISM AFTER $I^{131}$ THERAPY

Following radioactive iodine therapy, hypothyroidism may occur early or late, and may be transient or permanent.

*Transient* hypothyroidism was observed in 46 patients in our series (40 in the "diffuse" group, 6 in the "nodular" group). The duration of the hypothyroid phase was from 2 to 14 months. The PBI and 24-hour $I^{131}$ uptake values in one such case is charted in Fig. 6. Desiccated thyroid was given to many of these patients when their hypothyroidism developed, but was later discontinued; usually this was done on the clinician's advice, but sometimes on the patient's own initiative. It is quite possible that a number of our "permanent" hypothyroid patients now receiving desiccated thyroid therapy are actually no longer hypothyroid, but no attempt has been made to ascertain the extent of this possibility (e.g. by TSH administration, or by the withdrawal of therapy).

The incidence of *permanent* hypothyroidism (of all degrees) after $I^{131}$ therapy is depicted in Fig. 7. It can be seen that a total of 88 patients (or 16.3% of all cases) had serum protein-bound iodine values below the normal range, and thus were considered "hypothyroid". However, many of these patients had no symptoms or signs suggestive of hypothyroidism, other than mild fatigue in most instances; these patients had serum protein-bound iodine values only slightly below the normal range. Their $I^{131}$ uptakes were either slightly subnormal or in the low normal range. Their fatigue often responded to desiccated thyroid therapy in those cases in which it was utilized. Nine such patients (reported elsewhere) were given multiple injections of TSH* to determine whether an elevation of thyroid indices would occur. In none was there a significant response to TSH, thus placing these cases in the "low-reserve thyroid" category described by Jefferies.[36] This group tends to belie the "all or none" general rule whereby after $I^{131}$ therapy a patient may become totally hypothyroid or may become euthyroid, but should not settle in an "in-between" mild hypothyroid state. Although such a rule seems to apply to the majority of cases, it admits to several exceptions.

There was a significant difference between the "toxic nodular" group and the "diffuse" group in regard to the incidence of hypothyroidism, as well as to the degree of hypothyroidism after treatment. Of the "diffuse" group 17.7% developed permanent hypothyroidism, as against 11.7% of those with toxic nodular goitres. Of great importance was the

*TSH was kindly provided by Nordic Biochemicals Ltd., Montreal, as Thyrotron. (This material caused a marked increase in thyroid indices when given to normal persons. It also produced elevations in the thyroid indices in *most* of 12 *euthyroid* patients two to three years after $I^{131}$ therapy for hyperthyroidism.)

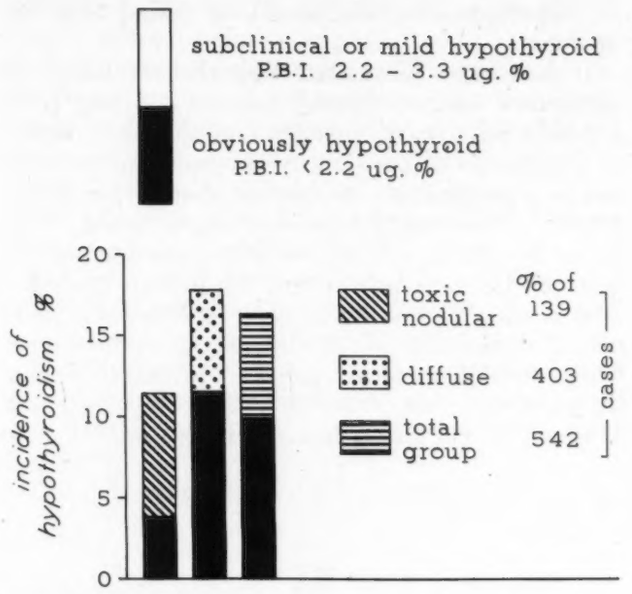


Fig. 7.—Incidence of hypothyroidism (all degrees) after $I^{131}$ therapy. This chart includes only those patients considered *permanently* hypothyroid.

observation that only 3.7% of the "toxic nodular" group had *obvious* hypothyroidism, as compared with 11.8% of those with diffuse thyrotoxic goitre. On the basis of clinical assessment alone, only the latter patients should perhaps be considered as having "true" hypothyroidism. In this case the total hypothyroid incidence after $I^{131}$ treatment could be considered to be 9.8% (see Fig. 7). A number of patients, almost always from the "diffuse" group (Fig. 8), have developed hypothyroidism years after treatment. Since some of our patients have been followed up for comparatively short periods, there will be an increased myxedema rate as time passes.

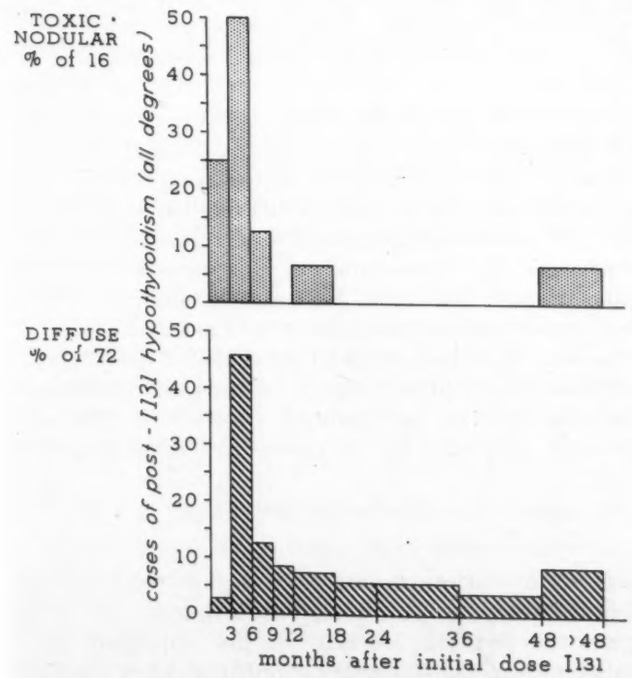


Fig. 8.—Time necessary to become permanently hypothyroid after $I^{131}$ (all degrees of hypothyroidism). Only two patients in the toxic nodular group became hypothyroid after the six-month interval (after $I^{131}$ therapy); both of these were very mild cases. In the "diffuse" group, conversely, late-onset hypothyroidism was often marked.

In the literature the incidence of hypothyroidism varies widely. Some of this variation has been a result of the difficulty in classifying hypothyroidism. Clark's[37] incidence of 20% hypothyroidism after treatment with $I^{131}$ included very mild cases of lowered thyroid function, as well as those with transient hypothyroidism.

On the other hand, Silver[3] has reported an incidence of only 3% hypothyroidism after $I^{131}$ therapy. Generally, results fall between these two extremes. Some authors have found no cases of hypothyroidism in patients with toxic nodular goitre.[1, 34] Recent articles have stressed the appearance of hypothyroidism years after therapy.[1, 26, 32, 34, 38]

Table IV summarizes the incidence of hypothyroidism after $I^{131}$ therapy from the literature.

TABLE IV.—INCIDENCE OF HYPOTHYROIDISM AFTER $I^{131}$ THERAPY FROM PREVIOUS REPORTS (EXPANDED FROM CASSIDY AND ASTWOOD'S TABLE)*

| *Authors* | *Euthyroid patients No. of cases* | *Hypothyroidism No. of cases* | *Total No. of cases* |
|---|---|---|---|
| Cassidy and Astwood[32] | 171 | 29 | 200 |
| Sheline and Miller[34] | 257 | 52 | 309 |
| Blomfield *et al.*[26] | 460 | 60 | 520 |
| Chapman and Maloof[1] | 478 | 42 | 520 |
| Albright[39] | 319 | 8 | 327 |
| Werner[38] | 447 | 78 | 525 |
| Nicholson *et al.*[40] | 103 | 4 | 107 |
| Balls *et al.*[41] | 147 | 33 | 180 |
| Hamwi and Goldberg[42] | 103 | 18 | 121 |
| MacGregor[43] | 126 | 24 | 150 |
| Clark and Rule[37] | 522 | 106 | 628 |
| Nadler *et al.*[44] | 61 | 11 | 72 |
| Rinkoff *et al.*[45] | 136 | 6 | 142 |
| Beierwaltes and Johnson[46] | 280 | 50 | 330 |
| Williams *et al.*[20] | 89 | 3 | 92 |
| McCullagh[47] | 578 | 64 | 642 |
| Miller *et al.*[48] | 89 | 10 | 99 |
| Wayne[49] | 80 | 8 | 86 |
| Rall *et al.*[50] | 88 | 28 | 116 |
| Seed and Jaffe[51] | 163 | 28 | 191 |
| Bauer and Blahd[52] | 100 | 6 | 106 |
| Green[93] | 122 | 26 | 148 |
| Rubenfeld *et al.*[94] | 270 | 24 | 294 |
| de Gennes *et al.*[106] | 110 | 21 | 138 |
| DeGowin *et al.*[107] | 307 | 31 | 338 |
| Lamberg *et al.*[108] | 114 | 21 | 144 |
| Totals | 5720 | 789 | 6525 |

*A similar table pertaining to toxic nodular goitres only was published by Eller *et al.*[105].

## DURATION OF TIME NECESSARY FOR THE DEVELOPMENT OF PERMANENT HYPOTHYROIDISM (FIG. 8)

After $I^{131}$ therapy, hypothyroidism usually makes its appearance between the third and ninth month (Fig. 8). However, hypothyroidism occurred in a small number of patients two to six years after treatment. Undoubtedly hypothyroidism will occur even later than this, and will continue to alter the incidence of post-$I^{131}$ myxedema. This emphasizes the need for at least yearly follow-up for all patients so treated.

Some of the instances of late hypothyroidism (more than two years after treatment) occurred in patients who became temporarily hypothyroid shortly after therapy, returned to a euthyroid state, and later became permanently hypothyroid.

### FACTORS INVOLVED IN THE PRODUCTION OF HYPOTHYROIDISM

It has already been mentioned that *clinical* hypothyroidism is an unusual feature in the toxic nodular group, for the reasons stated. Analysis of the age, sex, duration of illness, severity of illness, dosage of radioactive iodine, number of doses administered (Fig. 9), and previous antithyroid

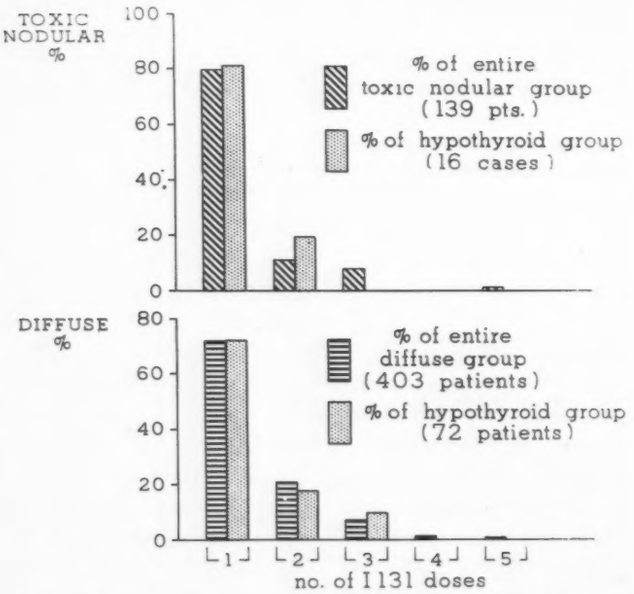


Fig. 9.—Number of doses of $I^{131}$ in entire group and in those becoming hypothyroid (all degrees of hypothyroidism). Multiple doses of $I^{131}$ did not appear to increase the incidence of hypothyroidism. With each dose, the incidence of consequent hypothyroidism was virtually the same.

therapy (Table V) in the hypothyroid group revealed no significant differences from those who had become euthyroid. Patients with small goitres had a higher incidence of hypothyroidism than expected (Fig. 10). Post-thyroidectomy recurrent hyperthyroidism was associated with a much higher incidence of post-$I^{131}$ hypothyroidism than was anticipated (Fig. 10) in the diffuse group.

In general these results are in agreement with the findings of others. Cassidy and Astwood[32] found that their incidence of hypothyroidism did not relate to gland size, while Blomfield *et al.*,[26] using scanning as a guide, found that the incidence of hypothyroidism decreased as gland size increased.

It has been speculated that the formation of antibodies against thyroid tissue (resulting from $I^{131}$-induced thyroid damage) might be a factor in the genesis of post-$I^{131}$ hypothyroidism, by leading to a continuing autoimmune destruction of the gland.[56] However, preliminary unpublished work in our laboratory has not indicated any correlation between the presence or titre of antithyroglobulin after use of $I^{131}$ and the occurrence of hypothyroidism. It is possible that studies of the complement-fixing antibody against a thyroid antigen other than thyroglobulin, as described by Belyavin and Trotter,[57] might show such a relationship.

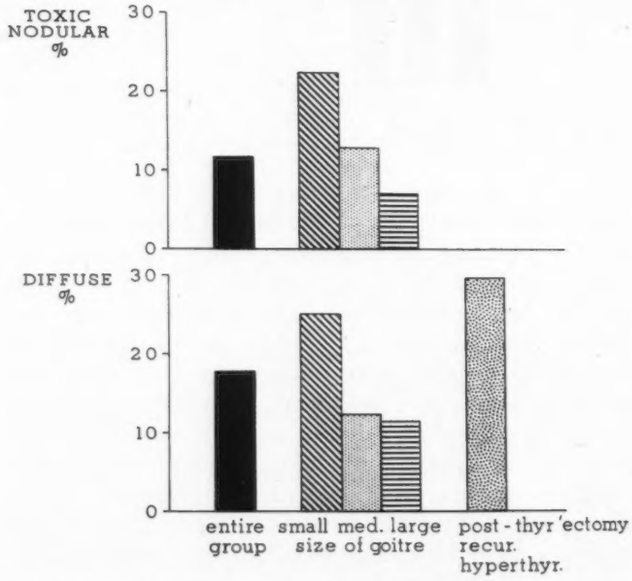


Fig. 10.—Hypothyroidism (all degrees) after $I^{131}$ therapy in various sizes of goitre and in recurrent hyperthyroidism. It should be noted that in the toxic nodular group there were 10 cases of post-thyroidectomy recurrent hyperthyroidism, but none of these later developed hypothyroidism.

Another factor worthy of consideration is the rate of "spontaneous" hypothyroidism during the course of untreated hyperthyroidism. Although there are no recent data pertaining to this incidence, Sattler[15] in 1907 recorded numerous examples of this occurrence. In the course of his review of this phenomenon he cited Murray,[16a] who described the appearance of myxedema in 9 cases during the course of the disease in 40 untreated hyperthyroid patients. Hypothyroidism under such circumstances may be due to autoimmune destruction. This is strongly suggested by the results of Doniach *et al.*[95]

### UNUSUAL VARIATIONS IN RESPONSE TO $I^{131}$ THERAPY

Certain variations in response to radioactive iodine therapy have already been noted: (1) most cases of hyperthyroidism simply subsided into euthyroidism (with single or multiple doses), either gradually or quickly; (2) most of the remainder fell "through" the euthyroid stage to hypothyroidism, although some patients remained in a

TABLE V.—HYPOTHYROIDISM (ALL DEGREES) AFTER $I^{131}$ THERAPY IN PATIENTS PREVIOUSLY GIVEN ANTITHYROID DRUGS

| | *Nodular (37 cases)* | *Diffuse (95 cases)* |
|---|---|---|
| No. of cases hypothyroid | 4.0 | 15.0 |
| % | 10.8% | 15.8% |

euthyroid state for considerable periods (even years) before becoming hypothyroid; (3) a stage of temporary hypothyroidism with subsequent recovery was noted in 46 patients; after remaining euthyroid for many months or years, nine of these patients developed permanent hypothyroidism.

There was, additionally, a small group of patients who manifested responses different from those mentioned above: (4) 29 patients (all with diffuse goitre) showed an initial benefit from use of $I^{131}$ with attainment of a euthyroid state, and subsequently *rebounded into hyperthyroidism once again*. This occurred invariably within the first four to seven months after the dose of radioactive iodine, and there were no *late* recurrences in this series.

TABLE VI.—CHIEF CAUSES OF DEATH IN PERIOD AFTER $I^{131}$ THERAPY AND TIME INTERVAL

| | *1st week* | *2-4 week* | *4-8 week* | *8-12 week* | *3-6 mos.* | *6-9 mos.* | *9-12 mos.* | *12-18 mos.* | *18-24 mos.* |
|---|---|---|---|---|---|---|---|---|---|
| Myocardial infarction | 1 | 1 | 2 | | 2 | 1 | | | |
| Congestive heart failure | 1 | | | | | | 1 | 1 | |
| Pneumonia | 1 | | | | | | | | |
| Cerebrovascular accident | 1 | | 1 | 1 | 1 | | | | |
| Suicide | | 1 | 1 | | | | | | |
| *Neoplasm:* carcinoma lower end esophagus | | | | | 1 | | | | |
| Bronchogenic carcinoma (onset preceded treatment) | | | | 1 | | | | | |
| Leukemia (discovered 3 mos. post-$I^{131}$) | | | | | | | | 1 | |
| Myasthenia gravis (onset preceded treatment) | | | | | | 1 | | | |

Of these 29 patients, 18 were given further doses of $I^{131}$ because of their return to a hyperthyroid state. However, (5) 11 of these 29 patients, after rebounding from a euthyroid state to one of hyperthyroidism, subsequently *regained their euthyroid state* spontaneously, thus requiring no further treatment. (6) One of the latter group who showed an early fall to euthyroidism, rebound hyperthyroidism, and later spontaneous return to euthyroidism, finally developed permanent hypothyroidism. (7) Eleven patients actually went through a phase of temporary mild hypothyroidism before rebounding to hyperthyroidism; eight of these were given additional doses of $I^{131}$, while (8) three patients spontaneously attained a euthyroid state without retreatment. (9) One of the latter group, who had rebounded from a transient hypothyroid state to hyperthyroidism, then spontaneously became hypothyroid despite the fact that no $I^{131}$ was given during the phase of rebound hyperthyroidism. The patients showing these unusual responses will be reported elsewhere in more detail. Some of these variations in therapeutic response have been noted by other authors.[103]

### *Deaths after Radioactive Iodine Therapy*

In this series, 21 patients died within two years of $I^{131}$ treatment. The causes of death and clinical summaries are presented in Table VI. In many of these cases it was clear that radioactive iodine was not a factor in the cause of death. In others, it was difficult to ascertain whether the therapy played any part in precipitating final illness. In all of those dying of vascular accidents (either cerebral or myocardial), there was a previous history of severe vascular disease. Some of these deaths were very shortly after $I^{131}$ therapy, while others were after a euthyroid state had been reached. Therapy obviously was not an aggravating factor in the latter cases, while in the former group their deaths were *not* associated with any obvious clinical, biochemical, or pathological evidence of radiation thyroiditis with its resultant possible exacerbation of hyperthyroidism.

In two cases the question of thyroid crisis was considered by the attending physicians. One patient was very seriously ill with pneumonia and heart failure before therapy, and progressed unfavourably after therapy, dying six days after $I^{131}$ treatment. Autopsy revealed severe generalized bronchopneumonia (for which no antibiotics had been given), as well as myocardial scarring. No evidence of thyroiditis was found pathologically. Thus, while it was perhaps unwise to treat this patient with $I^{131}$ without having pretreated him with antithyroid therapy, there is little more than coincidence to implicate therapy as a contributing cause of death. The other patient, an elderly Chinese, was likewise very ill with heart failure before treatment, but was given only 2.0 mc. of $I^{131}$, a very small dose. He similarly showed a continued deterioration, although one week after $I^{131}$ therapy his PBI appeared to be lower than its initial values. Signs of pneumonia and heart failure, as well as hyperpyrexia and diarrhea (chlortetracycline-induced?), were present. Although no autopsy was obtained, it seems unlikely that such a small dose of $I^{131}$ was a substantial factor in this situation, particularly when the PBI level had not risen. As in the previous case, it would have been wiser to pursue a more cautious course in treating such an ill person, treating him first by antithyroid drugs.

The two suicides were committed by previously depressed persons, and had no apparent relationship to therapy. The death from myasthenia gravis was also unrelated to therapy. In another patient the onset of bronchogenic carcinoma preceded treatment. The carcinoma of the lower end of the esophagus in one patient had no relationship to therapy.

One death from leukemia occurred in this series, but it should be noted that this patient's symptoms were manifest three months after treatment. This

appears to be too short an interval to suggest an etiological relationship, and will be discussed further under "Biological Hazards".

While it is not clear how many, if any, of these deaths were truly influenced by radioactive iodine therapy, it is apparent that elderly patients who have evidence of vascular disease should be given a course of antithyroid drug therapy prior to administration of radioactive iodine. This has become our practice.

In summary, the deaths in this series were generally of older people who suffered from other diseases, chiefly vascular. Many of these patients would have been considered very poor risks for thyroidectomy, thus making comparisons with surgical mortality rates difficult. More important, most of these deaths were clearly not related to therapy, while in the remaining few the relationship was based on coincidence. A clear cause-and-effect relationship could not be clearly established.

*Pathological Changes in Thyroid Gland after Radioactive Iodine Administration*

Only a small amount of pathological material was collected from this group of patients. Thus it cannot compare with the experience of Chapman and Maloof,[1] who examined specimens of thyroid tissue from 60 patients at varying intervals after $I^{131}$ therapy. Our own material shows changes similar to those previously described: hypertrophy of acinar cells, irregularity of size and shape of the nuclear

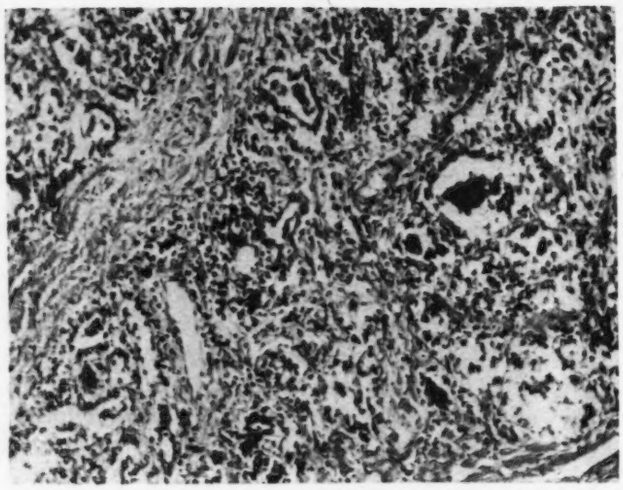

Fig. 11.—Section of a thyroid gland taken 3 months after $I^{131}$ therapy. Note the disruption of the follicle architecture, and the inflammatory changes. Colloid surrounded by phagocytes is seen, similar to the "pseudo-giant cells" of subacute thyroiditis.

structure with altered chromatin pattern, and fibrosis. In one specimen obtained three months after use of $I^{131}$, histiocytes were seen surrounding colloid in disrupted follicles, simulating the "pseudo-giant cells" of subacute thyroiditis (Fig. 11).

Maloof[58] has provided evidence suggesting that the cellular hypertrophy is secondary to pituitary stimulation rather than a direct effect of radiation.

*(To be concluded)*

*Note: The complete bibliography will be published with the final instalment of this report.*

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## EHRLICH-HATA REMEDY FOR SYPHILIS

(Reprinted from the *Canadian Medical Association Journal*, 1: 88, 1911)

The most important recent work in syphilis is to be credited to Ehrlich and his co-workers, Bertheim and Hata. The remedy which they have devised is now well known by the term "606".

A brief historical résumé may be of interest in tracing the steps which have led to the production of this new remedy. At the outset it may be said that Ehrlich had made 605 unsuccessful attempts to produce a remedy which would be active against the *Treponema pallidum*; with the 606th attempt came success, hence the title "606". As is well known, Ehrlich has for many years carried on very exact experiments, which have led to the preparation of "606". Interested in stereochemistry and therapeutics, he conceived the idea of developing a so-called "chemicotherapy", by preparing various synthetic compounds, whose formulae he could arrange, and re-arrange, by the substitution of certain radicals for those already present; such preparations, it was hoped, would be parasitotropic without being organotropic; that is to say, substances which would fix themselves in a specific fashion to the causal organism and kill it without in any way interfering with the function of the organ invaded. Ehrlich hoped in this way to obtain what he has called a "therapia sterilisans magna".

This work had taken a very definite direction since it had become known that certain protozoan infections were amenable to treatment with arsenical preparations. Salmon, in 1907, noted that atoxyl and other arsenical preparations were useful in the treatment of syphilis. It was soon shown, however, that, owing to the marked toxic action of atoxyl, it would not be available in the treatment of syphilis generally, and its use was quickly abandoned. Other preparations of arsenic, however, were suggested. Among these were the so-called "arsenpraparate" of Laveran and Loeffler, the dyes "brilliantgrün" of Wendelstadt, and "trypanrot" of Ehrlich. All these substances were given with the idea of producing an "inner disinfection", in cases of protozoan or bacterial infection.

When it had become evident that atoxyl would not be of use in the treatment of syphilis, Ehrlich thought of introducing acetic acid into the atoxyl molecule, giving rise to the preparation arsacetine. This substance, however, was found to be very toxic also. The next arsenical preparation, hectine, prepared by Mouneyrat, and used also by Balzer, was then tried. It showed a very remarkable activity against luetic lesions, and appeared to be less toxic than atoxyl or arsacetine. No cases of optic nerve trouble were reported from its use. Ehrlich then prepared another compound which has been used by Alt and other German syphilographers until the appearance of "606". It was arsensophenylglycine. This new remedy, "606", is dioxydiamido-arsensobenzol.—J. G. FitzGerald, M.D., Lecturer in Bacteriology, University of Toronto.

# REVIEW ARTICLE

## LES VIRUS DANS LES INFECTIONS DES VOIES RESPIRATOIRES

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### LA DEUXIÈME PARTIE

### RÉSULTATS PERSONNELS

DANS UN précédent travail nous avons tracé, en lignes générales, le problème des virus dans les infections des voies respiratoires. Nous continuons ici avec nos résultats personnels.

A l'Hôpital Sainte-Justine, nous avons commencé à rechercher de façon adéquate les Adénovirus vers le mois de septembre 1958. Nous avons utilisé les cellules Hela et chaque échantillon, soit le lavage de gorge, les sécrétions oculaires ou les selles, fut inoculé sur cette culture de tissu et 3 passages de 10 jours chacun[49] ont été pratiqués avant de considérer la recherche négative pour la présence d'Adénovirus. En plus, la recherche des anticorps de groupe, fixateurs du complément, a été faite sur un sérum précoce et un sérum tardif dans les cas où il fut possible d'obtenir ces deux sérums.

Durant la période de september 1958 à décembre 1958, au laboratoire, nous avons isolé plus fréquemment le virus de la poliomyélite et exclusivement le type I; en même temps que cette recrudescence de la poliomyélite, nous obtenions des réactions positives pour les hémagglutinines à froid et aussi nous isolions assez fréquemment des Adénovirus.

Nous avons relevé les cas étudiés au laboratoire concernant les infections dues à ces trois virus et nous avons comparé l'incidence des isolements positifs pour les Adénovirus chez les patients investigués pour poliomyélite et parmi les cas étiquetés Pneumonie primitive atypique.

Durant la période de juin 1958 à juin 1959, période que l'on peut considérer préépidémique en regard de la vague épidémique de l'été 1959, 66 patients ont été investigués au point de vue isolement et sérologie quant aux virus poliomyélitiques. Sur ce nombre, il y eut 23 cas de poliomyélite ou l'isolement fut positif pour le virus type I. De plus la sérologie seule fut positive chez plusieurs autres cas de paralysie type poliomyélite. En se basant sur les deux épreuves, il y eut 38 cas de poliomyélite sur les 66 patients dont 32 du type I, 2 du type II et 4 du type III.

La sérologie nous démontre, malgré le groupe particulier de cette étude, que 10 patients ne possédaient aucun anticorps neutralisant pour les trois virus de la poliomyélite. En plus, 14 autres patients ne possédaient aucun anticorps pour le virus type I; ce qui donne un total de 24 patients, soit 36% susceptibles de contracter la poliomyélite type I dans l'avenir.

On voit que le virus de la poliomyélite type I augmentait dans la population, vu la grande fréquence d'isolement du virus de la poliomyélite, et seulement du type I, et que d'autre part, il existait de nombreux enfants qui n'avaient eu aucun contact soit de façon naturelle ou artificielle avec le virus non seulement du type I, mais aussi des deux autres types.

Les tentatives d'isolement des virus poliomyélitiques à partir du liquide céphalo-rachidien furent vaines dans 10 cas. Le virus poliomyélitique fut isolé 22 fois à partir d'échantillon de matières fécales, et 7 fois à partir du lavage de gorge. De plus, dans ce groupe, nous avons isolé chez 7 patients un Adénovirus, et la recherche des anticorps fixateurs du complément pour les Adénovirus fut positive chez seulement 4 patients sur 17 investigués. Dans cette catégorie, il y eut isolement d'Adénovirus chez 5 patients présentant une symptomatologie caractéristique de la poliomyélite avec parésie ou paralysie et confirmée par un isolement positif du virus poliomyélitique chez un cas, et par la présence d'anticorps neutralisants chez les 4 autres. Les deux autres patients, où il y eut isolement positif d'Adénovirus, présentaient, l'un une hémiplégie droite avec signes de souffrance cérébrale à l'hémisphère gauche à l'électroencéphalographie; et l'autre une encéphalite avec signes méningés et signes de souffrance cérébrale diffuse. Parmi ces 7 patients, les deux derniers, et un cas parmi les 5 précédents, n'ont présenté aucun anticorps fixateur du complément pour les Adénovirus. Ce manque de relation est-il réel, ou est-il dû à un manque de mise au point des techniques? ceci nous laisse en doute sur la valeur étiologique de ces isolements.

Parmi les maladies autres que la poliomyélite et les infections à Adénovirus dont souffraient les autres enfants étudiés du point de vue de la poliomyélite, on y rencontre des syndromes divers, dont la grande majorité donne aussi des manifestations soit paralytiques, méningées ou encéphalitiques. Il y eut deux cas de Guillain-Barré, un cas d'encéphalite post-ourlienne, deux cas de méningite aseptique dont l'un avec isolement de Coxsackie A, un cas de séquelles de névrite diphtérique.

Si nous passons au groupe de pneumonies primitives atypiques à hémagglutinines à froid et agglutinines au Streptococcus MG positives, on note au tableau III que sur 99 patients chez qui ces recherches ont été exécutées, 30 patients ont donné des résultats positifs, c'est-à-dire, hémagglutinines à froid supérieures ou égales à 1/64, ou agglutinines au Streptococcus MG supérieures à 1/20. La plupart donnaient une image radiologique con-

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TABLEAU III.—PNEUMONIE PRIMITIVE ATYPIQUE

| | | Pneumonie | Bronchite | Autres |
|---|---|---|---|---|
| 99 cas | 39—0 à 5 ans | 20 (59%) | 14 (41%) | 5 |
| | 60—5 ans et plus | 41 (73%) | 15 (27%) | 4 |

| Mois et années | No. de cas | Positif | R.X. poumons | | | Age (ans) | For. blanche | | Titre moyen | | Recherche adenovirus | | Anticorps adenovirus | | Serum tardif |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Base | Haut | Bronches | Moyenne | Norm. | Elevée | H.F. | M.G. | Gorge | Selles | 1er sérum | 2ième sérum | Moyenne jours |
| 1958 Sept. | 7 | 2 | 2 | | | 10 | 1 | 1 | 96 | 20 | 1 | 0 | 1 | 1 | 25 |
| Oct. | 11 | 5 | 4 | 1 | | 8½ | 4 | 1 | 153 | 38 | 3 | 3 | 3 | 2 | 27 |
| Nov. | 8 | 3 | 3 | | | 9 | 1 | 2 | 245 | 87 | 3 | 2 | 1 | 3 | 26 |
| Déc. | 14 | 7 | 5 | | 2 | 8 | 4 | 3 | 119 | 100 | 3 | 3 | 2 | 4 | 21 |
| 1959 Janv. | 25 | 9 | 8 | 1 | | 7½ | 3 | 6 | 117 | 41 | 3 | 3 | 3 | 3 | 30 |
| Fév. | 10 | 0 | | | | | | | | | | | | | |
| Mars | 12 | 1 | 1 | | | 10 | 1 | | 64 | 20 | | | | | |
| Avril | 6 | 0 | | | | | | | | | | | | | |
| Mai | 3 | 2 | 1 | 1 | | 6½ | 1 | 1 | 96 | 25 | 1 | 1 | 1 | 1 | 12 |
| Juin | 2 | 0 | | | | | | | | | | | | | |
| 1959 Janv. | 1 | 1 | | | B.-P. 2 côtés | 7 mois* | 1 | | 16 | 10 | | | | | |
| Total | 99 | 30 | 24 | 3 | 3 | | 15 | 14 | | | 14** | 12 | 11 | 14 | |

* Sœur de 7 ans a fait pneumonie atypique en même temps.
** 16 investigués pour adénovirus sur 30.

forme à cette pathologie. Il est à noter que ces patients avaient un âge supérieur à 5 ans, sauf un patient ayant 7 mois et inclus comme positif en se basant sur l'enquête ou les notions épidémiologiques. En effet, ce petit patient a présenté une symptomatologie clinique identique, et ceci dans le même espace de temps, que sa sœur âgée de 7 ans, laquelle a présenté une convalescence beaucoup plus longue et dont son sérum donnait les taux d'anticorps suivants: hémagglutinines à froid 1/128 et 1/64 et agglutinines au Streptococcus Mg 1/40 et 0. Malheureusement, il n'existe à l'heure actuelle aucun moyen applicable de routine pour l'isolement du virus P.A.P. et par conséquent aucun moyen de déceler et de déterminer le taux des anticorps spécifiques. Cependant, on a prouvé la présence d'un virus distinct[50] et d'anticorps spécifiques dans ces pneumonies au moyen de la technique indirecte des anticorps fluorescents.[51] Certains auteurs disent que ce virus serait sensible aux antibiotiques[31] et à la Streptomycine, par conséquent lors des essais d'isolement au laboratoire, on doit éviter l'introduction d'antibiotiques dans les techniques utilisées et avoir recours à la filtration en vue de se débarasser des bactéries présentes. Ces pneumonies atypiques à hémagglutinines à froid, se rencontrent surtout à la fin de l'été et à l'automne, et toutes les épidémies rapportées concernent des adultes ou des adolescents.[52, 53]

Parmi les 30 cas diagnostiqués comme P.A.P. dans notre étude, la recherche directe ou indirecte des Adénovirus fut pratiquée chez 16 patients. Parmi ces derniers, il y eut 2 isolements positifs pour les Adénovirus et 6 réactions positives (y compris les 2 cas avec isolement positif) pour la présence d'anticorps fixateurs du complément. Ce qui donne un pourcentage de 38% de positivité pour les Adénovirus dans ce groupe. Chez un patient l'Adénovirus type 3 fut isolé, avec les titres de 1/16 - 1/128 pour les anticorps fixateurs du complément et 1/512 - 1/256 pour les hémagglutinines à froid. Chez l'autre l'Adénovirus type 2 fut isolé avec les titres de 1/16 - 1/32 pour les anticorps fixateurs du complément et 1/64 pour les hémagglutinines à froid et 1/160 pour les agglutinines au Streptococcus MG. Chez les quatre autres patients, les titres d'anticorps fixateurs du complément pour les Adénovirus étaient les suivants: 1/8; 1/8-1/64; 1/8-1/16; 1/16-1/16. Il y eut, par consequent, chez deux patients une augmentation de 4 fois du taux d'anticorps pour les Adénovirus, ce qui prouve dans ces cas une étiologie double, à Adénovirus et à virus P.A.P. Quant aux autres, l'étiologie double est discutable.

D'autre part, chez 25 patients investigués pour la présence d'anticorps hémagglutinants à froid, et agglutinants le Streptococcus MG et qui se sont avérés négatifs et chez lesquels des recherches virologiques ont été exécutées en vue d'une étiologie probable à Adénovirus, les résultats suivants ont été obtenus. Parmi ces 25 patients, 14 présentaient une radiographie suggestive d'atteinte du parenchyme pulmonaire. Il fut possible d'isoler chez 4 patients un Adénovirus et dans 5 autres cas, une réaction sérologique positive à la fixation du complément fut obtenue vis-à-vis de l'antigène de groupe des Adénovirus. Ce qui donne un pourcentage de 36% de positivité pour les Adénovirus. Dans ce groupe, un seul patient âgé de 7 ans, sans isolement d'Adénovirus mais ayant les anticorps fixateurs suivants 0 - 1/16 - 1/32 et présentant une radiographie compatible avec une pneumonie atypique, est fortement suggestif d'étiologie à Adénovirus. Trois autres patients plus jeunes que 5 ans, avec atteinte du parenchyme pulmonaire, et dont l'un en plus présentait une conjonctivite, peuvent être considérés comme atteints de pneumonie virale d'étiologie à Adénovirus: les trois ont eu un titre d'anticorps stable ou unique à 1/32,

TABLEAU IV.—PHARYNGO-CONJONCTIVITE

| Mois et années | No. | Age | Isolement | | Adeno. F.C. anticorps | | PR8-Lee-Q-Psitt. | Pharyngite Ad.cervicale | Conjonctivite | | Poumon | S.N.C. | Diarrhée | Eruption | Amygdales | T° | G.B. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Selles | Gorge | 1er sérum | 2e sérum | | | dr. | g. | | | | | | | |
| 1958 Sept. | 300 | 10 ms | Adéno. 3-7 | 0 | 0 | | | ++ | ++ | ++ | ++ | ++++ | | | — | 102 | 19,300 |
| Nov. | 387 | 7 ans | Adéno. | Adéno. 3 | 0 | 128 | | + | ++++ | ++++ | +++ | + | | | ++ | 104 | 8,300 |
| | 404 | 2 ans | Adéno. 2 | 0 | 64 | 128 | | + | +++ | | +++ | + | + | | + | 100 | 3,800 |
| Déc. | 393 | 11 ans | Adéno. 3 | — | — | | | + | | +++ | + | +++ | + | | — | 100 | 10,500 |
| 1959 Jan. | 427 | 11 ms | Adéno. | Adéno. 2 | 0 | | | + | + | + | +++ | | | | + | 101 | 6,500 |
| | 436 | 9 ans | Adéno. 1 | 0 | 16 | 32 | 0-0 Herpès 8-64 | + | ++ | ++ | ++ | +++ | | | — | 102 | 39,100 |
| | 442 | 6 ans | Adéno. 2 | Herpès | 16 | 16 | Herpès 32-128 | + | + | + | +++ | 0 | | | ++ | 104 | 26,900 |
| Fév. | 456 | 1 an | 0 | 0 | 32 | 32 | 0-0 | ++ | ++ | ++ | +++ | | | + | + | 102 | 14,500 |
| | 459 | 11 ans | Adéno. 3-7 | 0 | 32 | 32 | | 0 | +++ | +++ | + | | + | | — | 100 | 7,800 |
| | 464 | 5 ans | 0 | 0 | 4 | 4 | | ++ | + | + | 0 | +++ Epilepsie | Doul. | + | + | 100 | 12,100 |
| Mars | 477 | 1 an* | Adéno. 2 | 0 | 2 | 64 | 0-0 | ++ | +++ | +++ | + | | | | + | 101 | 13,200 |
| | 478 | 3 ans* | Adéno. | Adéno. 2 | 2 | 32 | 0-0 | ++ | +++ | +++ | + | | | | + | 101 | 8,200 |
| | 502 | 1 an | 0 | 0 | 0 | 8 | Lee 2-0 | ++ | +++ | +++ | + | | | | — | 101 | |
| Mai | 568 | 2 ans† | 0 | 0 | — | | | ++ | + | + | +++ | + | | + | + | 103 | 12,100 |
| | 569 | 4 ans† | Adéno. | 0 | 0 | 0 | 0-0 | ++ | + | + | +++ | | | + | ++ | 102 | 12,200 |
| Juin | 588 | 1 an | Adéno. 3-7 | — | 0 | 0 | 0 0 | ++ | ++ | ++ | +++ | | | | ++ | 103 | 12,000 |
| Août | 757 | 11 ans | Adéno. 3 | Strepto. A | — | | | ++ | ++ | ++ | | + | Doul. | | + | 103 | 8,200 |
| | 836 | 6 ans | — | Adéno. | — | | | ++ | ++ | +++ | + | +++ | Doul. | | — | 103 | 9,600 |
| Sept. | 1108 | 11 ms | Adéno. 3-7 | 0 | | | | + | ++++ Adéno. 3-7 | ++++ | | | | | — | 104 | 4,300 |

NOTES EXPLICATIVES DES QUATRE DERNIERS TABLEAUX.

Le titre d'anticorps dans les sérums est exprimé par la réciproque de la dilution des sérums.

*Dans les pharyngites:*
+ = indique une pharyngite et
++ = indique en plus une adénopathie cervicale.

*Dans les conjonctivites:*
+ = indique une hyperhémie des conjonctives.
++ = indique un écoulement séreux en plus.
+++ = indique un écoulement séro-purulent en plus.
++++ = indique un œdéme palpébral.

*Dans les poumons:*
+ = toux.
++ = toux et dyspnée.
+++ = indique radiographie pulmonaire et signes de bronchite.
++++ = indique une atteinte parenchymateuse.

*Dans le S.N.C.:*
+ = irritabilité, convulsions.
++ = Somnolence; EEG positif; L.C.R. fait et négatif.
+++ = Signes méningés; L.C.R. fait et négatif.
++++ = L.C.R. présente albumine ou cellules augmentés.

*Amygdales:*
+ = indique présence d'amygdales.
++ = amygdalectomie dans le mois courant.

et deux ont donné un isolement positif pour les Adénovirus, à savoir les types I et 5. Parmi les 5 autres patients, 2 cas ont eu un isolement positif (Adénovirus 3-7; 5) avec les taux fixateurs suivants: 1/8; -; les 3 autres cas avaient ces taux: 1/32 - 1/32; 1/16 - 1/16; 1/16 - 1/16. Il est peut-être difficile d'incriminer scientifiquement les Adénovirus dans ces derniers cas, cependant la formule leucocytaire normale ou légèrement élevée accompagnée de symptômes respiratoires et de température est en faveur d'étiologie virale. Par contre, dans ce groupe à hémagglutinines à froid et agglutinines à Streptococcus MG négatif, deux cas positifs pour la Grippe B, n'ont montré dans leur sérum aucune présence d'anticorps fixateurs du complément pour les Adénovirus.

Maintenant, si on laisse de côté, les isolements d'Adénovirus dans les cas de pneumonies primitives atypiques, de poliomyélite et qu'on examine les cas où il y a eu recherche et mise en évidence de réactions positives pour les Adénovirus seulement, on peut classer arbitrairement ces syndromes en 4 catégories: les pharyngo-conjonctivites, les pharyngites, les pneumonies, enfin les méningo-encéphalites.

L'étude des pharyngo-conjonctivites nous démontre que les Adénovirus isolés appartiennent aux types 2, 3, 3-7. Il est reconnu maintenant que le type Adénovirus 2 peut occasionner des conjonctivites. Ces conjonctivites peuvent varier d'une simple hyperhémie à un œdème palpébral: ce qui est indiqué dans le tableau IV par + à ++++. Les cas présentaient pour la plupart, une pharyngite avec rhinorrhée et une accentuation des images hilaires et des traînées broncho-vasculaires accompagnée de toux. La dyspnée ne fut rencontrée dans aucun cas. De rares cas ont présenté une diarrhée[54] ou des douleurs abdominales et de très rares cas, une éruption cutanée.[55] La formule leucocytaire était légèrement élevée aux

TABLEAU V.—PHARYNGITE

| Mois et années | No. | Age | Isolement | | Adeno. F.C. anticorps | | PR8-Lee Q-Psitt. | Pharyngite | Poumons | S.N.C. | Diarrhée | Eruption | Amygdales | T° | G.B. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Selles | Gorge | 1er sérum | 2e sérum | | | | | | | | | |
| 1958 Oct. | 305 | 8 ans | 0 | 0 | 8 | | PR8=4 | + | +++ | | | | | 101 | 7,800 |
| | 306 | 5 ms | Adéno. | 0 | 0 | | 0-0 | ++ | + | | | | | 100 | 16,400 |
| | 315 | 2 ans | Adéno. 3 | 0 | — | | | + | +++ | | | + | + | 104 | 7,400 |
| | 340 | 2 ans | Adéno. | Adéno. 2 | — | | | ++ | ++ | + | | | + | 104 | 12,200 |
| Nov. | 359 | 15 ms | Adéno. 3 | Strepto. A | 0 | 0 | 0-0 | ++ | +++ | | + | | | 104 | 24,100 |
| Déc. | 417 | 1 an | Adéno. 2 | 0 | 0 | | | + | +++ | | + | | + | 101 | 5,000 |
| 1959 Jan. | 431 | 10 ans | 0 | 0 | 32 | 16 | 0-0 | + | | | | | + | 100 | 9,000 |
| | 439 | 8 ms | Adéno. | Adéno. 2 | 0 | 0 | 0-0 | + | ++ | | | | | 103 | 8,400 |
| Fév. | 469 | 8 ans | Adéno. 3 | 0 | 0 | 128 | | ++ | | ++ | +doul. | | + | 103 | 20,600 |
| Mai | 557 | 3 ans | Adéno. | 0 | 64 | 128 | 0-0 | ++ | + | | | | + | 102 | 7,400 |
| | 573 | 3½ ans | Adéno. 3-7 | 0 | | | | ++ | | | + | | + | 101 | 11,600 |
| | 605 | 3 ans | 0 | 0 | 4 | 0 | 0-0 | + | | | | | + | 100 | 8,700 |
| Juin | 613 | 1½ ms | Adéno. 2 | Adéno. | 0 | 0 | 0-0 | ++ | | + | + | | | 102 | 8,600 |
| | 626 | 10 ms | Adéno. | Adéno. 2 | 4 | 4 | 0-0 | ++ | +++ | | | | | 103 | 7,300 |
| Juil. | 642 | 6 ans | Adéno. ? | | — | | | + | | +++ | | | | 103 | 10,700 |
| Août | 761 | 16 ans | Adéno. ? | | — | | | ++ | + | +++ | +doul. | | + | 103 | 10,800 |
| | 775 | 9 ans | Adéno. 3 | | 0 | 64 | | ++ | | +++ | doul. | | | 103 | 9,400 |
| | 958 | 9 ans | 0 | Adéno. 3 | — | | | ++ | | +++ | | | + | 103 | 13,100 |
| Sept. | 1068* | 10 ans | Adéno. 3 | | | | | ++ | | +++ | | | 0 | 102 | 7,200 |
| | 1093* | 8 ans | Adéno. 3 | | 0 | 32 | | ++ | | +++ | doul. | | | 103 | 4,500 |

alentours de 12,000. Sauf deux cas associés à une gingivo-stomatite à virus herpétique, il semble certain ici, que les Adénovirus, avec ces symptômes cliniques classiques soient la cause évidente de ces infections malgré la faillite de la réponse sérologique dans certains cas.

Les pharyngites étudiées sont aussi nombreuses que les pharyngo-conjonctivites; la plupart ont eu un isolement positif pour les Adénovirus. Dans ce groupe on note dans le tableau V des cas de pharyngites présentant des symptômes ressemblants à la poliomyélite où il y a eu ponction lombaire pratiquée à cause de douleurs localisées soit dans le dos ou la nuque et avec certaine contracture antalgique. Ces cas furent étiquetés cliniquement comme Poliomyélite abortive, mais le laboratoire n'a pu confirmer ce diagnostic. On note aussi que plusieurs cas présentaient des douleurs abdominales et de la diarrhée. Un cas, le No 417, a présenté un symptomatologie clinique ressemblant à la laryngite striduleuse. Comme on le voit, le dépistage de ces infections par la réaction de fixation du complément seulement, nous aurait révélé très peu de cas dans notre étude. Cependant, les formules leucocytaires normales et la température assez élevée dans nombre de cas nous laissent soupçonner une infection d'origine virale. Alors, il faut en conclure que si ces pharyngites sont dues aux Adénovirus, il y a eu un manque de corrélation entre les isolements et les réactions sérologiques obtenues. Il faut savoir, cependant, que la fixation du complément se base sur le principe qu'il existe un antigène commun spécifique de groupe pour tous les Adénovirus. Toutefois, si ceci se produit dans la plupart des cas, il faut savoir qu'il y a eu des études expérimentales faites en vue du typage des Adénovirus au moyen de la fixation du complément. Ceci veut dire que l'exécution de la recherche des anticorps fixateurs du complément, chez un patient, sera beaucoup plus fidèle et de

TABLEAU VI.—PNEUMONIE

| Mois et années | No. | Age | Isolement | | Adéno. F.C. anticorps | | PR8, Lee Q-Psitt. | Poumons | Pharyngite | Amygdales | Diarrhée | T° | G.B. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Selles | Gorge | 1er sérum | 2e sérum | | | | | | | |
| 1958 Nov. | 361 | 4 ans | 0 | Adéno. | 0 | 0 | 0-0 | B.-P. | + | + | | 102 | 8,800 |
| | 331 | 9 ms | 0 | Adéno. 2 | 16 | | | B.-P. base d. | + | | + | 104 | 17,800 |
| Déc. | C.I.V. 408 | 3 ms | Adéno. 2 | 0 | 2 | 0 | | B.-P. | | | + | 100 | 14,900 |
| 1959 Jan. | 423 | 1½ ms | Adéno. 5 | 0 | 0 | | 0 | Sommet g. | + | | + | 104 | 9,200 |
| Avril | 551 | 1 an | Adéno. 3-7 | 0 | 0 | 0 | 0 | A.H. péri-bronchite 2 bases | | + | | 100 | 6,300 |
| Juin | 616 | 14 ms | Adéno. | 0 | | | | Base g. | ++ | + | | 101 | 7,800 |

TABLEAU VII.—MENINGO-ENCEPHALITE

| Mois et années | No. | Age | Isolement | | Adéno F.C. anticorps | | PR8, Lee | CML,-EEE, EEW, STL. | L.C.R. | Somnolence | E.E.G. | Autres | Poumons | Pharyngite | Amygdales | T° | G.B. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Selles | Gorge | 1er sérum | 2e sérum | | | | | | | | | | | |
| 1958 Oct. | d.c.d. 350 | 2 ms | Adéno. 3 | 0 | | | | 0 | + | | + | Convulsions | +++ | + | + | 102 | 8,800 |
| Nov. | 383 | 3 ans | 0 | 0 | 64 | 64 | 0 0 | 0-0 | 0 | + | — | Parésie mem. inf. d. | + | + | ++ | 102 | 7,700 |
| Déc. | 414 | 1½ an | 0 | Adéno. 2 | 32 | | 0-0 | 0-0 | + | ++ | + | Convulsions | + | | | 105 | 39,300 |
| | 416† | 2½ ans | — | Adéno. 2 | 0 | | | | 0 | + | | Convulsions | ++ | | + | 100 | 7,400 |
| | 418† | 2½ ans | Adéno. | Adéno. 2 | 64 | | | | 0 | + | | | + | + | + | 103 | 9,400 |
| 1959 Jan. | T.B.? 434 | 7½ ans | 0 | | 64 | | 0 | 0 | + | ++ | + | Cécité | Calcification hilaire | | + | 100 | 6,300 |
| Fév. | 473 | 5 ans | Adéno. 3-7 | 0 | 0 | | | | + | + | 0 | Réhospitalisation Méningite pneumo. | + | ++ | + | 100 | 21,300 |
| | 474 | 3½ ans | 0 | 0 | 64 | | 0 | 0 | 0 | | 0 | Paralysie spasmo. mem. inf. g. | | | | 100 | 5,400 |
| Mars | 481 | 11 ans | 0 | 0 | 8 | 4 | 0 | 0 | 0 | + | + | Eruption | + | ++ | | 105 | 2,400 |
| Avril | 538* | 2½ ans | Adéno. 3 | 0 | 8 | 0 | 0 | | + | ++ | + | Convulsions Tremblement | | + | | 102 | 7,700 |
| | —* | 6 ans | — | — | | | | | | | | Doul. abdo. Eruption? | + | ++ | | 102 | 5,200 |
| | 544* | 6 ms | Adéno. 3 | 0 | 0 | | 0 | | 0 | | 0 | | +++ | ++ | + | 104 | 8,200 |
| Mai | 564 | 3 ans | Adéno. 2 | 0 | — | | | | | ++ | | Convulsions | | | | 99 | 15,400 |
| Août | 697 | 17 ms | Adéno. | 0 | — | | | | | + | | Fracture péronée | | + | | 100 | 5,200 |
| | d.c.d. 717 | 2 ans | 0 | | 0 | 16 | 0 | 0 | 0 | ++ | | Diarrhée Convulsions | + | | | 105 | 25,100 |
| | 787 | 5 ans | Adéno. 3-7 | | — | | | | 0 | ++ | +drt | Hémiplégie g. | | | | 100 | 5,100 |
| | 788 | 12 ans | Adéno. 3-7 | 0 | | | | | 0 | | | Doul. dos, nuque | | ++ | | 103 | 7,200 |
| Sept. | 1091 | 10 ans | Adéno. | | 0 | 16 | | | 0 | + | | Doul. dos, jambes | | + | + | 102 | 6,200 |

type plus élevé, si on l'exécute avec le type d'Adénovirus infectant le patient. De plus, pour confirmer cet énoncé, des études expérimentales ont démontré la présence d'anticorps fixateurs dans certains sérums avec l'emploi d'un type d'Adénovirus comme antigène et l'absence d'anticorps dans ces mêmes sérums avec l'emploi d'autres types comme antigène.

L'explication de nos réactions de fixations du complément négatives obtenues chez de nombreux patients hébergeant des Adénovirus pourraient ête à l'origine de l'emploi d'un antigène fixateur de groupe pas adopté aux souches isolées. Il nous est impossible de vérifier cependant s'il y a eu plus de réactions positives lorsque certains types d'Adénovirus étaient isolés car nous avons utilisé trois types, d'antigène fixateur du complément, différents. Nous avons d'abord utilisé un antigène commercial, puis antigène fourni par le gouvernement fédéral et ensuite nous avons utilisé notre propre antigène fabriqué à partir de l'Adénovirus type 6.

Les cas de pneumonie inclus dans le tableau VI n'ont pas eu de recherche pour les hémagglutinines à froid; tous ces enfants sont d'un âge inférieur à 5 ans et tous ont présenté un isolement pour les Adénovirus (type 2, 5, 3-7); on note ici de la toux et de la dyspnée; le cas No 616 présentait en plus une respiration difficile et bruyante. La formule leucocytaire est en général normale, sauf 2 cas où elle est franchement augmentée et est loin de faire soupçonner une infection virale, du moins primitive. De plus, 3 cas présentaient de la diarrhée. Les cas de pneumonie à Adénovirus[56-59] chez les enfants, rapportés dans la littérature et qui ont eu une issue fatale ont démontré la présence d'inclusions nucléaires identiques aux cas décrits par Goodpasture[60] en 1939.

Maintenant, ce qui est très peu rapporté dans la littérature, ce sont les atteintes du système nerveux central par les Adénovirus. L'étude faite par Bell et Rowe[61] durant une épidémie de pharyngo-conjunctivite et où le type 3 prédominait, démontre que beaucoup de patients présentaient de la somnolence au début de la période de convalescence. Dans notre étude nous avons relevé des patients présentant des syndromes méningés ou méningo-encéphalitiques et chez lesquels nous avons isolé des Adénovirus ou obtenu une réaction sérologique positive. Plusieurs avaient un liquide céphalo-rachidien anormal quant au nombre de cellules ou à la quantité d'albumine. Un grand nombre a présenté de la somnolence et même du coma, ce qui est indiqué par ++ dans le tableau VII.

Des chercheurs, entre autres Lépine,[62-63] ont rapporté des cas présentant une atteinte encéphalitique et où il existait de très fortes présomptions en faveur d'Adénovirus comme agent étiologique. Ceci n'est pas étonnant, car le virus de l'Influenza[64] lui aussi est reconnu pour causer des encéphalites. Dans notre série de cas présentant de telles manifestations, il y eut 2 décès dont un âgé de 2 mois et chez lequel un Adénovirus type 3 fut isolé. L'autre décès concernait un enfant de 2 ans qui a présenté les taux suivants à la fixation du complément pour les Adénovirus à savoir : 0 et 1/16.

## DISCUSSION

Il est connu que le diagnostic des maladies à Adénovirus peut se faire facilement par la réaction de fixation du complément pratiquée sur des sérums précoce et tardif, en utilisant un antigène de groupe.[65-66] En plus, les anticorps fixateurs du complément apparaissent avant les anticorps neutralisants. D'autre part la fixation de complément sur les sérums nous aide aucunement dans l'identification du type d'Adénovirus en cause, de même, les réponses hétérotypiques observées dans les sérums lors de ces infections, nous empêchent dans les tests de neutralisation de conclure au sérotype exact d'Adénovirus infectant le patient. Pour arriver à cette identification, il faut absolument isoler et typer l'Adénovirus contenu dans les produits pathologiques.

Dans cette étude, les réactions de fixation du complément pour les Adénovirus ont été souvent négatives, même dans des cas où il y avait grande présomption d'obtenir une réaction positive. Grayston[49] rapporte qu'il y a corrélation entre un isolement précoce et facile des Adénovirus dans les produits pathologiques et une infection plus sévère ainsi qu'une meilleure réponse immunologique. D'autre part, certains auteurs[67] ont démontré que des sérums de patients présentaient des anticorps fixateurs du complément pour les Adénovirus, si on employait tel type au lieu d'autres types, dans la préparation de l'antigène. De plus, il est rapporté dans la littérature[68] qu'on peut parvenir à l'identification de type d'Adénovirus, en employant la réaction de fixation du complément et dans ce cas le type est indiqué par la plus grande capacité que possède l'Adénovirus isolé à fixer le complément en présence de titre connu d'immuns-sérums expérimentaux. Par conséquent, pour obtenir dans les sérums de patients des taux plus adéquats et plus élevés, on doit utiliser plusieurs antigènes fixateurs du complément ou utiliser l'antigène correspondant au sérotype isolé chez le patient.

Il est intéressant de noter dans cette étude que les infections pulmonaires à Virus P.A.P. semblent se limiter aux enfants au-dessus de 5 ans, tandis que les pneumonies à Adénovirus se sont produites chez des enfants en bas de 5 ans. De ceci, il ne faut pas conclure que le virus P.A.P. n'infecte pas les enfants au-dessous de 5 ans; un example dans notre étude d'un cas de 7 mois, nous laisse soupçonner une telle éventualité.[69] Est-ce que les jeunes enfants présentent une symptomatologie différente ou une maladie bénigne qui serait la cause d'une réponse faible en anticorps hémagglutinants à froid ou agglutinants le Strepto MG? L'isolement du virus P.A.P. nous donnera sûrement une réponse quant à l'incidence de ce virus dans ce groupe d'âge. D'autre part, les pneumonies à Adénovirus rapportées dans la littérature et concernant les enfants nous démontre la fréquence d'infections pulmonaires, surtout chez les nourrisons et les très jeunes enfants. D'autre part, les atteintes méningo-encéphalitiques par les Adénovirus, quoique très bénignes comme pronostic dans la plupart des cas présentaient à un certain moment de leur évolution, des symptômes alarmants à la fois pour le médecin et pour les parents. Cette atteinte méningo-encéphalitique semble exister, vu les signes de souffrance diffuse cérébrale relevés à l'électro-encéphalographie et l'anormalité du L.C.R. se traduisant surtout par une légère augmentation de cellules ou une augmentation de l'albumine. Quelles sont les séquelles éventuelles de ces infections virales sur le cortex cérébral? Il est impossible d'y répondre actuellement.

Les patients qui ont présenté soit un isolement, soit des anticorps fixateurs positifs pour les Adénovirus étaient au nombre de 85 dans notre étude. La moitié de ces cas est survenue dans le groupe d'âge de 0 à 3 ans. Il est certain qu'un grand nombre d'Adénovirus isolés étaient liés à la symptomatologie observée; cependant dans quelques cas, la relation de cause à effet est douteuse vu le manque de réponse sérologique; il faut penser aussi à une élimination prolongée de ce virus, due à une infection clinique déjà lointaine et non actuelle et par conséquent à une infection latente[70] ou à des porteurs sains de virus, cette dernière explication n'étant cependant pas admise par les virologistes.

## RÉSUMÉ

Dans ce travail, l'auteur présente les divers virus susceptibles de causer des infections au niveau du tractus respiratoire. Parmi ces virus, les Adénovirus et le virus de la pneumonie atypique primitive (P.A.P.) ont été étudiés spécialement. Les P.A.P. au nombre de 30 cas ont été étudiés au point de vue clinique et au point de vue diagnostic de laboratoire. Ces pneumonies à virus se distinguent des pneumonies à Adénovirus, par le développement d'hémagglutinines à froid et agglutinines au Streptococcus M.G. dans le sérum des patients et aussi par son incidence exclusive dans le groupe d'âge supérieur à 5 ans. Les complications bactériennes dans ces infections sont très rares et par conséquent le pronostic est toujours bon.

Quant aux infections à Adénovirus, des isolements nombreux ont été effectués dans des formes cliniques diverses et il n'y eut pas de corrélation entre le type isolé et la forme clinique observée. Les types d'Adénovirus isolés étaient les suivants: type 2, 3, 5, et intermédiaire 3-7; quant à ce dernier type, il est certain qu'il ne s'agissait pas du type 3; d'autre part, vu que les immuns-sérums type 3 et 7 neutralisaient au même titre ces virus, l'auteur croit qu'il s'agit du type intermédiaire décrit par les auteurs japonais.

Les infections causées par les adénovirus, sont survenues pour la plupart chez des enfants plus jeunes que 5 ans. L'auteur rapporte des cas de pharyngites, de pharyngo-conjonctivite, de pneumonies ainsi que des cas avec atteinte méningée ou méningo-encéphalitique. Il y eut assez fréquemment un manque de corrélation entre l'isolement et la sérologie, et l'auteur essaie de trouver une explication à cette constatation.

## SUMMARY

*Virus Infection of the Respiratory Tract*

Several viruses capable of causing respiratory tract infection are described in two consecutive articles. Among these the adenovirus and the primary atypical pneumonia viruses (P.A.P.) especially have been studied. Thirty cases of P.A.P. have been examined both from the clinical and laboratory points of view. Atypical pneumonia may be differentiated from that caused by an adenovirus by the production of cold and streptococcus MG agglutinins in the serum of the patient and also by its exclusive incidence in the group of patients above five years of age. Bacterial complications of these infections are very rare, consequently the prognosis is always favourable.

In regard to adenovirus infection, numerous isolations have been made from several clinical forms, and no correlation has been found between the type isolated and the clinical form observed. The adenovirus types isolated were 2, 3 and 5, and the intermediate type 3-7. The latter is asserted to be different from type 3, but since the immune sera of type 3 and 7 equally neutralized these viruses, it is believed that the intermediate type described corresponds to that reported by Japanese authors.

Adenovirus infections occur mostly in children below five years of age. Pharyngitis, pharyngoconjunctivitis, pneumonia, meningitis and meningoencephalitis are also reported. The frequent lack of correlation between the isolated type and the serological findings is discussed.

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## RHEUMATISM AND SO-CALLED CHRONIC RHEUMATISM

(Reprinted from the *Canadian Medical Association Journal*, 1: 23, 1911)

In the list of complaints made by patients, "rheumatism" would take a high place, and in the list of diagnoses made by physicians, it would also be well up in the list. Patients come to us complaining of it, but, whether we are justified in letting them depart with such a diagnosis is a question for discussion. Certainly it is a diagnosis which is usually satisfying to the patient, but whether it should be satisfactory to the physician is another matter. In this faculty of satisfying the patient it shares the honour with "too much uric acid" and "something wrong with the liver". For the southern states we might add, "a touch of malaria". However, such a diagnosis is about the same as that said to have been given by Sir William Gull to the insistent wife of a patient when no certain opinion could be given: "Madam, your husband has a cachexia."

It is particularly to the use of the terms "rheumatism" and "chronic rheumatism" that attention is here directed. To what is the term "rheumatism" applied? If enquiry is made into this question, we are struck at once by the fact that it is employed in various ways. Thus, it is used to designate the disease known as rheumatic fever and also as a synonym for arthritis, as, for example, gonorrheal "rheumatism". Now it is very evident that a term cannot be employed to designate the whole and a part of the whole with any clearness of meaning. We cannot well use it to designate any form of arthritis and also a particular disease often characterized by a special form of arthritis. A recent example is found in a journal to which we look as a guide in matters of correct usage; namely, the heading "Tuberculous articular rheumatism". Now, if the word "rheumatism" is here used as synonymous with arthritis, we have "tuberculous articular arthritis", which is absurd. If it is used as meaning rheumatic fever, surely no one believes that we have a tuberculous rheumatic fever. Actually, the article was one on tuberculous arthritis. Again, an article in one of the English journals was headed "Scarlatinal rheumatism". Can anyone tell from this title what is meant? It may be intended to represent a hybrid combination of scarlet fever and rheumatic fever (like the typho-malarial fever of the South), or arthritis in scarlet fever, or a particular kind of rheumatism. Then again, the term rheumatism is applied to many other conditions which have nothing to do with arthritis; for example, vague pains are often so designated.—Thomas McCrae, M.D., F.R.C.P., Associate Professor of Medicine, The Johns Hopkins University.

Canad. M. A. J.
Jan. 7, 1961, vol. 84

THE CANADIAN MEDICAL ASSOCIATION
JOURNAL
LE JOURNAL DE
L'ASSOCIATION MÉDICALE CANADIENNE

*published weekly by*
THE CANADIAN MEDICAL ASSOCIATION
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*(Information regarding contributions and advertising will be found on the second page following the reading material.)*

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## RETROSPECT

*If men could learn from history, what lessons it might teach us!*—Coleridge.

FIFTY years ago this month the *Canadian Medical Association Journal* was launched on a career of uninterrupted publication with the following eloquently simple proclamation by its original editor, Dr. Andrew (later Sir Andrew) MacPhail:

"The Canadian Medical Journal *which is issued on January 1st, 1911, is the official journal of the Canadian Medical Association. It is published in virtue of a resolution which was passed at the annual meeting in Toronto, in June, 1910. According to the terms of that resolution the finance committee have appointed an editor. They have entered into a contract with a publisher, and they have acquired the Montreal Medical Journal, which is now merged into the new publication.*

*"The Canadian Medical Association is an organization comprising all the provincial associations in Canada, governed by a constitution and by-laws, which were adopted at the annual meeting held in Montreal, September 11th to 13th, 1907. One of the objects for which the association was established is set forth in the following terms: 'The publication of such information as may be thought desirable in the form of a periodical journal, which shall be the Journal of the Association.'*

*"Accordingly,* The Canadian Medical Journal *is issued, as a medium for the expression of all that is best in Canadian medicine. For practitioners of general medicine, or in any special department of it; for workers in the laboratory or the hospital, a vehicle is offered, which goes wide afield, for the conveyance of fresh information, free comment, and sound opinion. There are at present in Canada many excellent journals, some of which are more or less local in character and circulation; and others which, for a variety of reasons, are more widely known.* The Canadian Medical Journal *will be scrupulously careful to distinguish itself from these publications, and so avoid any competition which might arise from similarity of methods; so that their interests may not suffer.*

*"It will be its aim to offer adequate means of publication, within the country, of material, some of which, at least, has hitherto been brought to the notice of the profession in English and foreign journals. If Canadian thought upon medicine is to make that impression upon the world, which its importance warrants, it must be concentrated in one channel. What that channel shall be remains for the thinkers themselves to decide."*

The pages of Volume 1, Number 1, reveal a fascinating glimpse of the medical scene as it unfolded in 1911, reflected in the "fresh information, free comment and sound opinion" of the thinkers of the day. In the vanguard of a procession of seven distinguished articles was a scholarly discourse on "The Ancient Foundations of Heredity" by A. B. Macallum, Professor of Biochemistry, University of Toronto. Thomas McCrae, M.D. (Toronto), F.R.C.P., Associate Professor of Medicine, The Johns Hopkins University, deplored the confused and hazy concepts of "rheumatism and so-called chronic rheumatism", though many ears have remained deaf to his message of common-sense throughout the succeeding half century. J. G. FitzGerald, then Lecturer in Bacteriology at the University of Toronto (and for many years the Dean of its Faculty of Medicine), expounded on the exciting new discovery of the Ehrlich-Hata remedy for syphilis, with its cabalistic designation "606". A series of articulate editorials, some profound and forceful, others of a simpler, "newsy" character, included a classical essay on "Style in Medical Writing" that the would-be author of today would do well to read and heed; indignant protestations over the derogatory reports on conditions in the Halifax Medical College and the medical school of Queen's University submitted by a certain Mr. Abraham Flexner to the Carnegie Foundation for the Advancement of Teaching; an intriguing commentary on "Caisson Disease in Canada"; and the announcement of recently negotiated reciprocity in medical teaching between the medical schools of McGill and Toronto Universities.

The tribulations and triumphs that have been the lot of the Canadian Medical Association and its Journal over the decades that followed have been sketched elsewhere on these pages by the facile pens of Drs. MacDermot, Routley and Kelly. As we celebrate the golden anniversary of publication it seems particularly appropriate to pay tribute to those who so auspiciously created this venture in Canadian medical journalism.

"Let us watch well our beginnings and results will manage themselves."

## THE GOLDEN ANNIVERSARY

### *A Message from the Editor of the World Medical Journal*

WHEN I and my friends, recruits to the medical profession, joined our national medical association twenty-five years ago, we did so primarily because it was the cheapest form of postgraduate education. It was the cheapest form of education because our association published and distributed to members for a small fee a weekly journal containing practically all that was necessary for the practitioner to keep in touch with medical progress in his country, and indeed much of value to the embryo specialist as well.

Times have changed, and it may be that young men join an association because of burning interest in "medical economics" or "public relations", two subjects unknown 25 years ago, but one suspects that many still feel a need to join because their association is the responsible national body for promoting their life-long education in the art and science of medicine. Nothing has yet supplanted the general medical journal in this respect, and the smallest and newest of medical societies is never happy until it has produced some publication, however humble, as a service to its members, as a symbol of their unity, and as a bond between them.

But a status symbol is all the better for being useful, and in looking back over the past half century the *Canadian Medical Association Journal* can justly claim to have been very useful indeed. At this time, it has a particular use not relevant to some other national journals. Ottawa has recently decreed that a Royal Commission should recommend measures which would "contribute to the further development of a Canadian identity through a genuinely Canadian periodical press". This is no academic enquiry but a practical study, so perhaps the Commission might like to take a look at the contribution which the *Canadian Medical Association Journal* has been making for fifty years to the development of a Canadian identity. May it in the fifty years to come continue to reflect the image of a truly Canadian medicine!

S. S. B. GILDER

## A FLOURISH OF GOLD TRUMPETS

### *A Message from the Editor of the Journal of the American Medical Association*

FIFTY YEARS of distinguished journalism is indeed an occasion for rejoicing. Your "kissin' kin" south of the border are happy to share in the festivities at this distance. For a period longer than I care to divulge, because of personal pride, I have held the *Canadian Medical Association Journal* in high esteem. Whenever the occasion demanded reference to an original communication, I was impressed with the quality of the scientific data presented as well as the composition of the contents. The impact of authority of the Canadian Medical Association in supporting the official publication has been complementary to the sound judgment of the members of the editorial staff who select, edit and publish the manuscripts. The Canadian Medical Association can be proud of the accomplishments of the bilingual publication that it has sponsored for half a century.

However, superseding all other agencies and individuals in such a venture as a medical periodical is the office of the editor, a pre-eminent position. It gives me great pleasure to take notice, tardy though it is without reason, of the recent change in incumbency. It has been my privilege to know Dr. Donald Graham since the completion of his formal medical training several years ago. I can vouch from personal contacts that he is a fine clinician, a capable investigator, and an experienced executive in medical administration. His talents in each category undoubtedly were responsible for his appointment to this important post.

The Canadian Medical Association and the *Canadian Medical Association Journal* are to be congratulated in having Dr. Graham as the editor on this, the fiftieth anniversary of its publication. It is flattering to me to have a physician of Dr. Graham's stature occupy a parallel position in Canadian medical journalism.

A toast to your Journal in its fiftieth year and to the new editor in his first year!

JOHN H. TALBOTT

## THE FIFTIETH ANNIVERSARY

### *A Message from the Editor of the British Medical Journal*

I HAVE been a constant reader of the *Canadian Medical Association Journal* for the past thirty years—a little more than half its lifetime. I have known the past three editors of your great journal, and know, too, that it is the quality of these men that has made the *C.M.A.J.* what it is and what it has become. It therefore gives me real and personal pleasure to say "Happy 50th birthday"! And if I may continue to be personal, may I say to the present distinguished occupant of the Editorial Chair that the first fifty years are the worst; though this does not mean that the next fifty will be free from toil and trouble. Heaven forbid!

However placid and calm is its final appearance, a journal—each number of it—is born out of strife—strife with proprietors, publishers, authors, advertisers, and readers. This is as it should be.

The face that Canadian medicine presents to its own profession and public at home—and of equal or even greater importance, to the profession and public in other countries—depends first and foremost, and to some extent exclusively, upon the *Canadian Medical Association Journal*. Therein is manifested the character of the Canadian doctor,

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the intellectual achievements of Canadian medicine, the integrity of your profession in its dealings with itself and with the great Canadian public. Each week your journal goes to press you commit in words that cannot be erased all these things, and much more. And an army of candid critics will be on their toes to point out to you the errors of your ways.

The freedom of the medical press is of supreme importance to a free profession, as important as the freedom of the national press is to the welfare and integrity of a free people. So long as this is maintained in the *Canadian Medical Association Journal* it will in its centenary year be able to look back at its fiftieth birthday with the same pride as you can now feel in looking back to your beginnings. In this exciting and responsible prospect the *British Medical Journal* wishes you all success and happy and arduous days.

HUGH CLEGG

# *Greetings from Journalistic Confrères*

### THE NEW ENGLAND JOURNAL OF MEDICINE

ON BEHALF of the Committee on Publications of the Massachusetts Medical Society and the editorial board of the *New England Journal of Medicine*, engaged already in the planning of an anniversary of our own publication, a year hence, it is a pleasure to extend greetings to the *Canadian Medical Association Journal* on the occasion of its fiftieth birthday.

Relations over the invisible, intangible fence that fails to divide us have been cordial. As an associate editor of this journal in 1928, I first met Dr. A. D. Blackader, your editor from 1919 to 1929, when he brought messages of good will to our hundredth anniversary as the *Boston Medical and Surgical Journal*.

A long time later, in 1955, when I was struggling with the responsibility of a weekly deadline, Ernest MacDermot brought his successor, Stanley Gilder, to discuss with me the problems that might be associated with semimonthly publication. The doubling of the circulatory beat of the *Canadian Medical Association Journal* was successfully achieved in the same year.

May the new editor find satisfaction in continuing the work and maintaining the standards that have been set!

JOSEPH GARLAND, Editor

### THE LANCET

WITH SO MANY journals in the world, the present system of publishing papers is inefficient as a means of bringing facts to all who need them. Sooner or later doctors and scientists will have to introduce some alternative by which reports of investigations are registered, recorded, and mostly circulated in abstract instead of being printed in full. But even when this happens, medicine will still have to have its general periodicals, which cover all sorts of medical subjects and are one of the chief means of holding the profession together. Though few read *all* the articles they publish, anyone who regularly looks at his weekly medical newspaper will be aware not only of how medicine is developing but of what other doctors are doing; and this is especially necessary in a big country and in one with diverse traditions. After fifty years, the *Canadian Medical Association Journal* is commonly taken for granted; but its interest and variety have made it immensely valuable as an integrating force in its own country, while for readers in other parts of the Commonwealth it displays the heartening likeness of our aims and hopes. The first fifty years are solid foundation for a great future.

T. F. FOX

### L'UNION MÉDICALE DU CANADA

LE JOURNAL de la "Canadian Medical Association" fête son 50ième anniversaire. Evènement heureux à la louange de ceux qui l'ont fondé et de ceux qui ont veillé à sa survivance et à son essor. Car il a incontestablement contribué à l'expansion et au progrès de la médecine canadienne. Les journaux médicaux sont nombreux de par le monde. On ne s'est jamais plaint qu'ils fussent surabondants. L'enseignement de la médecine, surtout sur le plan post-universitaire, s'effectue surtout par le journal. Il est actuel et est prodigué au rythme des travaux et des recherches. Le médecin est nécessairement maintenu en haleine et c'est ainsi qu'il peut par le truchement d'un journal sérieux, bien administré et averti, en somme fidèle à sa mission, entretenir et agrandir ses connaissances à l'allure rapidement évolutive de la médecine.

Tel fut le rôle rempli par le journal de la "Canadian Medical Association" pendant cinquante années.

"L'Union Médicale du Canada" dont la mission est semblable depuis 89 ans souhaitait, dans sa livraison de janvier 1911, la bienvenue au nouveau confrère et lui adressait ses meilleurs souhaits. Elle lui exprime en 1961 un témoignage de félicitations

et des voeux de plein succès dans ses initiatives en plus d'une longue vie d'oeuvres fructueuses.

ROMA AMYOT,
Rédacteur en chef

THE PRACTITIONER

IT IS with the greatest of pleasure that I send you our congratulations on the occasion of the fiftieth anniversary of the publication of the *Canadian Medical Association Journal*. A Golden Jubilee is always a particularly auspicious occasion and the Canadian Medical Association has every reason to be proud of the service it has received from you and your predecessors as editor of a journal which has now an international reputation.

In sending you the congratulations of *The Practitioner* on attaining your Golden Jubilee, we would add our very best wishes for the second half-century upon which you are now entering.

WILLIAM A. R. THOMSON,
Co-Editor

THE MEDICAL JOURNAL OF AUSTRALIA

THE EDITOR and Staff of the *Medical Journal of Australia* extend the most cordial of greetings and congratulations to the *Canadian Medical Association Journal* on the attainment of your fiftieth anniversary. The people of our two countries have long been linked by strong ties of both kinship and friendship, in which the members of the medical profession have shared. We therefore welcome the opportunity to add to the relationships between our Commonwealth and our elder sister Dominion of Canada, and to express hearty goodwill to the *Canadian Medical Association Journal*, with proper respect from the *Medical Journal of Australia*, which is your junior by four years.

RONALD R. WINTON, Editor

THE NEW ZEALAND MEDICAL JOURNAL

THE New Zealand Branch of the British Medical Association and the *New Zealand Medical Journal* congratulate with deep sincerity the *Canadian Medical Association Journal* on completing fifty years of successful publication. Your journal has attained wide recognition and in this remote country occupies a prominent position in our medical libraries. We know that the medical profession of Canada has ever been represented with dignity and authority while the highest standards of medical journalism have consistently been achieved. New Zealand doctors will wish all future success and strength to the *Canadian Medical Association Journal*.

J. O. MERCER, Editor

THE JOURNAL OF THE INDIAN MEDICAL ASSOCIATION

IT IS indeed gratifying to learn that the *Canadian Medical Association Journal* is marking its fiftieth anniversary with this issue. The half-century through which the Journal has come has been a period of great achievements in medical science and medical journalism, a period during which medicine has attained a sound scientific status throughout the world.

As the world tends to achieve oneness, medical science sheds its "systems" to synthesize a single body of knowledge. The epoch-making discovery of Banting and Best on the one hand and Susruta's rhinoplasty and the use of *Rauwolfia serpentina* on the other are all part of this synthesis. Nor must we forget the great teacher, Osler, whose writings have inspired two generations of practitioners not only in his own country but also in India and elsewhere.

I have much pleasure in congratulating the *Canadian Medical Association Journal* for its excellent work for five decades, and wish it many happy returns of its birthday.

Good luck and good cheer.

P. K. GUHA, Honorary Editor

THE CANADIAN JOURNAL OF SURGERY

THE EDITORIAL Board of the *Canadian Journal of Surgery* extends felicitations to its elder companion publication on the occasion of its fiftieth anniversary, congratulates it upon the service that it has rendered to Canadian medicine, and wishes it continued success in its efforts to disseminate scientific knowledge and to serve as a vehicle for news and opinion of interest to Canadian doctors.

ROBERT M. JANES,
Chairman, Editorial Board

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GREETINGS FROM THE CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES

THE Canadian Federation of Biological Societies, comprising the Canadian Physiological Society, Pharmacological Society of Canada, Canadian Association of Anatomists and Canadian Biochemical Society, offers to the *Canadian Medical Association Journal* congratulations and good wishes on the occasion of the celebration of the Journal's fiftieth anniversary.

E. H. BENSLEY, M.D.,
Honorary Secretary,
Canadian Federation of
Biological Societies.

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# MEDICAL NEWS IN BRIEF

## CARTILAGE AND BONE MARROW EXTRACT IN TREATMENT OF OSTEOARTHRITIS

From the University Clinic for Rheumatism and the Institute for Physiotherapy of the Kantonsspitals of Zurich comes a report on the treatment of osteoarthritis by extracts prepared from cartilage and cartilage plus bone marrow.

A double-blind therapy test was carried out on a total of 149 patients. Some of them received placebo, others injections of bone marrow plus cartilage extract and a third group cartilage extract alone. Injections are given at first daily, increasing the dose from 0.3 to 0.5 and 1 ml., and afterwards three times a week, for a total of twenty injections. No analgesics or local applications were allowed during that period, nor were patients encouraged to diminish their activities to any degree.

In reporting their results, Wagenhäuser, Hauser and Fellmann (*Schweiz. med. Wchnschr.*, 90: 1164, 1960) point out that they chose two forms of arthritis in which objective examination enabled them to judge the results of treatment. They selected arthritis of the knee and of the distal and proximal interphalangeal joints of the hand. There was good to very good objective and subjective improvement in 83% of the cases treated by extract of cartilage plus bone marrow and in 64% of those receiving only cartilage extract. They usually improved by the third week, but combining this treatment with physiotherapy brought faster results. Of the patients treated by placebo injection, 93% showed no objective improvement and 89% failed to experience any subjective improvement.

## PHENYLBUTAZONE AND LEUKEMIA

Six cases of leukemia, including acute, chronic, myeloid and lymphoid types, encountered in elderly males, all of whom had a history of recent use of phenylbutazone, have been reported by Bean (*Brit. M. J.*, 2: 1552, 1960). The possibility that the association between phenylbutazone administration and the development of leukemia may have been attributable to chance was noted. If, on the other hand, phenylbutazone did act as a leukemogen in these cases, this was the result of a dose and a duration of treatment that varied from 10 g. over a three-week period to several hundred grams over a period of four years. In one case there was a definite progression of hematopoietic changes from the time of administration of the drug to the development of frank myeloid leukemia 16 months later.

One of the unusual features of these cases was the bizarre clinical and histological picture presented by several of them. In those whose blood dyscrasia ran a more acute course the peripheral blood film and bone marrow morphology were atypical and difficult to interpret. Bone marrow aplasia and hemolysis were associated with the illness in at least three of the six cases. In five of the six, the leukemic phase was extremely short and treatment apparently produced at best only transitory improvement. Another feature upon which the author commented was the fact that three of these six patients had tuberculosis. It was observed that others have previously reported several cases in which caseous reactions followed the administration of phenylbutazone, though it is possible that this association, too, may have been fortuitous.

The author, commenting on the apparent increase in leukemia incidence reported by Court-Brown and Doll in 1959, observed that while these data could be interpreted in different ways, it seems reasonable to conclude that there has been an actual increase in acute leukemia, particularly in elderly persons. Court-Brown and Doll suggested that radiation exposure had played an important part in this increasing leukemia incidence. In the present series of six patients who developed leukemia after phenylbutazone administration, none had any previous exposure to therapeutic radiation. The author concludes his discussion with the thought-provoking comment that "all drugs or other substances known to be capable of causing agranulocytosis should also be suspected as possible causes of leukemia."

## POISONING BY MALATHION (ORGANO-PHOSPHORUS) INSECTICIDE

Malathion is a readily available insecticide, widely used in home gardens, and as such is a potential poison hazard. Such organo-phosphorus compounds may gain entry by the mouth, the respiratory system, or the skin, the toxicity varying with the particular organo-phosphorus compound absorbed. They exert their action in the body by inactivation of cholinesterase. While Malathion is one of the less toxic organo-phosphorus compounds, ingestion of a concentrated emulsion thereof may be fatal, as in the case recently reported by Paul (*New Zealand M. J.*, 59: 346, 1960). This patient, after accidental ingestion of a comparatively small amount of Malathion, reported to hospital where gastric lavage was performed immediately and atropine, 1/50 grain, was administered intramuscularly. Shortly thereafter, convulsions, respiratory embarrassment and cyanosis developed and the patient died about an hour and a half after ingestion of the chemical.

After skin absorption there is evidence of a cumulative activity involving a progressive cholinesterase inhibition, the red blood cell cholinesterase being destroyed before the plasma cholinesterase. The erythrocyte cholinesterase level appears to be the most reliable indication of chronic Malathion exposure. As symptoms may not appear until the cholinesterase levels have been depressed below 10% of normal, there is a narrow margin between levels productive of no symptoms and those causing death. Thus, a patient could be chronically exposed without apparent effect for many days, then suddenly manifest severe symptoms although exposure may be no greater than previously.

Current treatment consists in the administration of atropine and an antidote known as P2S as soon as possible, since fatalities occur as a rule within one-half to four hours after exposure.

*(Continued on advertising page 35)*

# COME TO MONTREAL IN JUNE!

FOR THE

## 94th ANNUAL MEETING OF

# THE CANADIAN MEDICAL ASSOCIATION

## JUNE 19-23, 1961

*Canadian National Railways*

**OLD AND NEW, SIDE BY SIDE—that's Montreal. In the heart of the city, the Queen Elizabeth Hotel, site of the 1961 Annual Meeting, looms in the background, and across the street is the Cathedral of Mary Queen of the World, a reduced replica of St. Peter's in Rome. In June, Dominion Square will be filled with evening folkdancers and outdoor art exhibits, all part of the unique atmosphere that marks Canada's largest city.**

### MEETING HIGHLIGHTS

The Scientific Program this year will concentrate on Teaching Sessions, which are designed to inform general practitioners of new developments in diagnosis and treatment. These will commence Tuesday morning, June 20, and will continue throughout most of the following two days. These sessions are in the nature of refresher courses and include panel discussions in medicine, surgery, pediatrics, anesthesia, obstetrics and gynecology.

The General Sessions, Wednesday and Thursday, will include three special speakers in medicine, anesthesia and psychiatry, and will be highlighted by the Lister Oration Thursday morning. Friday, June 23, has been set aside for Medical Economics day, and will include a number of addresses and panel discussions on medical services insurance and other economic matters of topical interest.

As in former years, there will be church services on the Sunday preceding the commencement of the Meeting.

All major sessions will be simultaneously translated into French or English.

The Annual General Meeting on Wednesday night will be the highlight of the convention. The incoming president, Dr. G. W. Halpenny, will be installed; His Excellency the Governor-General, Major-General Georges P. Vanier, will be invested with an Honorary Membership in the C.M.A.; and various Senior Memberships awarded. This event will be followed by the President's reception and dancing.

A full week of social events has been planned for your enjoyment. Monday evening will feature a wine-tasting party at which a number of domestic and imported wines may be tasted. The dinner for the General

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# BIENVENUE À MONTRÉAL
## le 19-23 JUIN, 1961

With the approach of the 94th Annual Meeting of the Canadian Medical Association, it gives me great pleasure to welcome you to Montreal.

The members of the Quebec Division look forward with enthusiasm to returning some of the kind hospitality which we have received in so many cities across Canada.

*W. Gordon Mitchell*

DR. G. W. HALPENNY

Our Committees have planned an interesting scientific and social program with many unusual features. Detailed accounts of this program will be published in subsequent issues of the Journal.

With governments and political parties attempting to solve the problems of medical care, the Canadian Medical Association needs the support of every doctor in Canada, if it is to offer the wisdom and the strength of a united leadership. We hope that there will be a large attendance on the day we have set aside for a full discussion of these problems.

May I extend my personal invitation to every member to be present at this Annual Meeting.

J'invite particulièrement mes confrères de langue française de tout le Canada à assister à ce 94e congrès annuel. Les programmes scientifiques et sociaux sont déjà complétés et je suis sûr que tous trouveront un grand avantage à y participer. Le colloque sur l'économie médicale sera d'une importance primordiale car la solution des problèmes que nous affrontons aujourd'hui peut affecter le sort de tous les practiciens du pays. Les membres de la Division du Québec s'efforceront, j'en suis certain, de recevoir comme il convient leurs confrères des autres provinces.

GERALD W. HALPENNY, M.D.,
*President-Elect*

The *Canadian Medical Association Journal* has kindly given me this opportunity to invite the doctors' wives from across Canada to the 94th Annual Meeting. A very warm welcome awaits you in Montreal.

The members of the Ladies' Committee look forward to meeting you, and their program has been specially arranged to allow you to enjoy our historical and

*W. Gordon Mitchell*

MRS. G. W. HALPENNY

cosmopolitan city. We feel that our planned events will be of unusual interest to everyone. Our Hospitality Centre will offer you a wide choice from among the innumerable attractions of Montreal, and our ladies will be happy to accompany you on shopping ventures if you so desire.

Built around Mount Royal, the mountain inside a city, Montreal has a special charm, much of which lies in the atmosphere created by its French founders. I am sure you will feel the enchantment of this unique city. It will give me great pleasure to welcome you in June.

Puis-je adresser une invitation particulière aux épouses des médecins de langue française? J'espère qu'elles assisteront en grand nombre à ce congrès. Le comité des dames sera enchanté de les recevoir et de leur aider à faire de cette visite dans la métropole canadienne, la deuxième plus grande ville française du monde, la plus agréable qui soit. Je vous souhaite personnellement la bienvenue et j'anticipe le plaisir de vous rencontrer à Montréal au mois de juin.

KAYE HALPENNY

# HOUSING APPLICATION FORM

## The Canadian Medical Association

## 94th ANNUAL MEETING - June 19 - 23, 1961

## MONTREAL, QUEBEC

Apply direct to the:

Reservations Manager,

Hotel.....

Address:.....

Please reserve the following accommodation (check): (All rooms have baths and/or showers.)

Single bedroom..... Twin bedroom.....

Suites for one person (bedroom and parlour).....

Suites for two persons (bedroom and parlour).....

Suites for four persons (2 bedrooms and parlour).....

Family Plan—no charge for children under 14.....

In view of the large attendance expected, it might be to your advantage to share a room with another member. Please mention below the names of the persons with whom you would like to share your accommodation; otherwise assignment will be suggested by the Committee on Arrangements.

I (we) will arrive in Montreal on June.....at.....A.M.....P.M.

I (we) will depart from Montreal on June.....at.....A.M.....P.M.

Travelling by: Air..... Train..... Automobile.....

NAMES OF PERSONS OCCUPYING ACCOMMODATION REQUESTED ABOVE:

.....

.....

ADDRESS(ES).....

.....

TELEPHONE No..... .....

N.B.—(1) A list of hotels and motels is shown on the following page with daily rates.

(2) Confirmation of housing will be made direct from hotel or motel.

**THIS WILL CONSTITUTE YOUR ADVANCE REGISTRATION FOR THE MEETING.**

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# HOTELS AND MOTELS AVAILABLE FOR THE ANNUAL MEETING

## Montreal, Quebec, June 19 - 23, 1961

*Daily rates*

THE QUEEN ELIZABETH:
Dorchester St. West,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $10.00 to $20.00 |
| Twin Bedrooms | 14.00 to 20.00 |
| Two-room Suite (parlour and bedroom) | 36.00 to 50.00 |
| Three-room Suite (parlour and bedroom) | 57.50 to 70.00 |
| Four-room Executive Suite (parlour, 2 bedrooms and dining room) | 90.00 to 110.00 |
| Family Type (studio double and deck beds) | 16.00 to 20.00 |
| Portable Bed for Additional Person at | 4.00 per day |

No charge for children 14 years of age and under, if sharing same accommodation as parents.

Free Parking.

THE SHERATON-MOUNT ROYAL HOTEL:
1455 Peel Street,
Montreal, P.Q.

| | |
|---|---|
| Room and Bath for one | $ 8.50 and up |
| Double Beds for two | 12.00 and up |
| Twin Beds for two | 13.85 and up |
| Suites for one person | 24.50 and up |
| Suites for two persons | 28.00 and up |
| Suites (2 rooms-parlour) for four | 44.00 and up |

Family Plan—Free Parking.

LAURENTIAN HOTEL:
Dominion Square,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $ 8.50 to $ 9.50 to $10.00 |
| Double Beds | 12.00 to 12.50 |
| Twin Beds | 12.50 to 13.00 |
| Suites for one or two | 21.00 |
| Suites for four | 36.50 |

*Daily rates*

WINDSOR HOTEL:
Peel Street,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $10.00 and up |
| Double Bedrooms (including twin beds) | 14.00 and up |

RITZ-CARLTON:
1228 Sherbrooke Street West,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $13.00 to $15.00 |
| Double Bedrooms (including twin beds) | 16.00 to 18.00 |

ROYAL EMBASSY:
Peel and Sherbrooke Streets,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $13.00 and up |
| Double Bedrooms (including twin beds) | 18.00 and up |

QUEEN'S HOTEL:
700 Windsor Street,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $ 6.00 to $ 7.00 and $ 8.00 |
| Double Bedrooms (including twin beds) | $10.00 to $11.00 and $12.00 |

MOTELS:

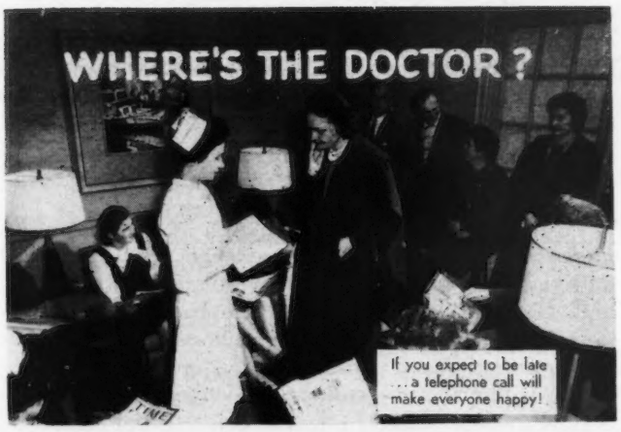
MOTEL PIERRE:
2375 Laurentian Blvd.,
Montreal, P.Q.

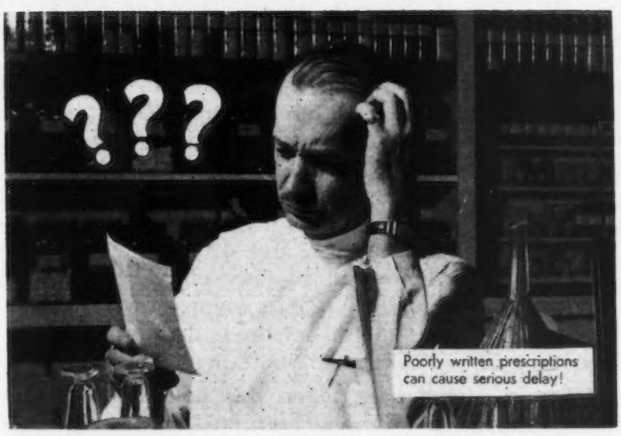
| | |
|---|---|
| Single Bedrooms | $ 7.50 |
| Double Bedrooms (including twin beds) | 9.50 and up |
| Twin beds | 10.50 and up |

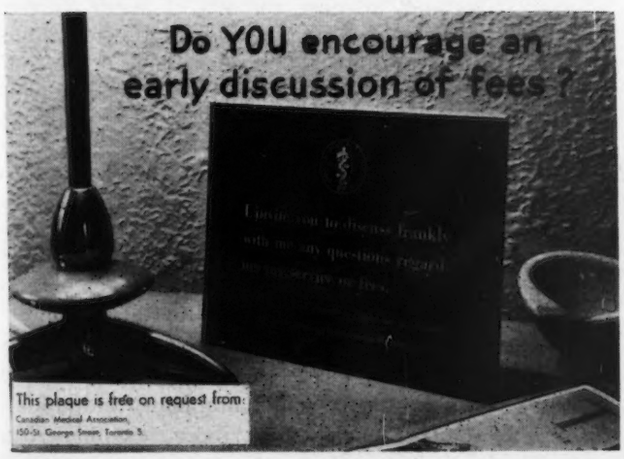
AU LUCERNE MOTEL:
4950 Sherbrooke Street East,
Montreal, P.Q.

| | |
|---|---|
| Single Bedrooms | $12.50 and up |
| Double Bedrooms (including twin beds) | 14.00 and up |

# DOCTOR–PATIENT RELATIONS




Do YOU encourage an early discussion of fees?
This plaque is free on request from:
Canadian Medical Association,
150 St. George Street, Toronto 5.

By the very nature of their profession, doctors are in the bright spotlight of public opinion every day. Irrespective of where they are, or what they are doing, their actions are immediately transformed by the public into opinions, and eventually into attitudes.

As a profession, medicine has set a standard second to none. Apart from outstanding accomplishments that are achieved daily, the diligence and skill of Canadian doctors in their day-to-day practice have gained the respect and admiration of their patients. On the other hand, the public has been educated to expect a continuation of high medical standards, and the man on the street is critical of the slightest deviation.

In the main, it is not the quality of medical treatment that fosters adverse opinions; but rather it is the little things such as the manifestation of consideration for their thoughts, feelings and emotions, that patients seek.

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# MEDICAL MEETINGS

## THE FIRST INTERNATIONAL CONFERENCE ON CONGENITAL MALFORMATIONS

THE FIRST International Conference on Congenital Malformations (sponsored by The National Foundation) was held in London, England, July 18-22, 1960, and attended by over 400 delegates from 26 countries. Experts from a wide variety of disciplines, including embryology, virology, genetics, epidemiology, teratology, physiology, obstetrics, and pediatrics, presented papers and took part in panel discussions on the causes of malformations and their medical impact.

The "Theme Address" was delivered by Dr. George W. Corner, Historian and Affiliate of The Rockefeller Institute, and formerly Director of the Department of Embryology of the Carnegie Institution of Washington. Dr. Corner pointed out that Ambroise Paré, in the sixteenth century, classified human abnormalities as those resulting from (1) the intervention of God or the Devil, (2) bad seed ("crooke-backt produces crooke-backt"), and (3) poor maternal environment (imagination, "faulty maternal postures" or "straightness of the womb"). Today no one who has studied the problems concerned with congenital malformations believes that such defects result from the intervention of the Devil or through the mother's incurrence of the wrath of God, but there are those who wonder if any better explanations are forthcoming. Dr. Corner felt that, although there was still considerable controversy over the relative importance of genetic and environmental factors in the causative mechanisms underlying maldevelopment, there had been tremendous advances in the understanding of the subtlety and complexity of these factors.

He then discussed the evolution of ideas regarding the etiology of congenital abnormalities in man, beginning with the realization by eighteenth century anatomists that congenital deformities represent modification of the normal pattern of embryonic growth rather than random disorderly growth. At the turn of the present century, Mall, who was influenced by the studies of Loeb, Stockard and E. B. Wilson on the experimental production of defects in non-mammalian forms, felt that most human abnormalities resulted from a poor uterine environment. Gradually, with a growing awareness of the importance of the action of genes in the control of development in lower organisms, and the realization that many of the "abnormalities" of the uterus described by Mall to buttress his thesis were actually normal phases of the menstrual cycle, the genetic explanation of congenital malformations almost completely displaced the environmental hypothesis. The belief that all human abnormalities resulted from the action of genetic factors received a jolt in the early 1940's with the discovery of the teratogenic action of the rubella virus and the early experiments in mammalian experimental teratology, and the pendulum of medical opinion began to swing again to the environmental side. With the present interest in chromosomal aberrations in man a new phase of the cycle might be underway. Although Corner still believes that the majority of congenital abnormalities in man result more from genetic than environmental causes, he feels that this cyclic history of theories of etiology should caution against any sweeping generalities in this regard.

### *Incidence*

In the first session, Dr. Erhardt (New York City Department of Health) outlined the epidemiological and statistical pitfalls facing investigators in the field, and discussed the merits and drawbacks of the prospective and retrospective approaches to the problem. He appealed for a closer alliance of the statistician and the clinician in studies of congenital malformation. Professor Lamy (Paris) pointed out that the simple matter of counting abnormalities in a population presented great difficulties, resulting chiefly from the lack of agreement on the definition and classification of congenital defect, and the manner in which data are presented in the literature. Keeping these problems in mind, Professor Lamy gave the following figures: (1) The incidence of major malformations discovered at term in both liveborn and stillborn infants is roughly 1 to 1½%. (2) This figure increases to 4 to 5% if there is a follow-up of one year, and will be higher still if malformations discovered in later childhood or even adulthood are included. (3) In countries where accurate vital statistics are maintained, malformations account for 15 to 20% of infant mortality.

A most stimulating paper was presented by Professor McKeown (Birmingham) on "Sources of variation in the incidence of malformations". These sources were environmental in nature, and included maternal age, birth order, season of birth, social class, and secular variation. Anencephalus, for instance, shows a conspicuous association with season of birth, primogeniture and lower social class, and McKeown suggests that further enquiry into this type of relation may reveal the environmental factors involved in the causation of anencephaly, which are, at present, the ones most likely to be controllable.

### *Intrinsic Factors (Genetic)*

In speaking on "Some genetic aspects of congenital defect", Dr. J. V. Neel (Michigan) pointed out that fully penetrant dominant and recessive genes, well-established environmental factors, and chromosomal aberration account, at most, for 40% of major congenital defects. The factors responsible for the remaining 60%, comprising most of the serious major malformations, are still largely unknown, but the following observations may contribute to their understanding. (1) Racial studies, although rather limited in nature, reveal the striking fact that although the overall incidence of defects in each racial group is of roughly the same order, the rates of specific defects differ significantly between races. (2) Defects recurring in families are usually type-specific. (3) The frequency of defects amongst offspring of consanguineous mating is significantly elevated over that of the general population, and this applies particularly to rare, or complex and multiple malformations. (4) The number of individuals with more than one defect is more common than

would be expected by chance alone, and the pattern of defects reflects, in exaggerated form, the pattern of defects in the population of which such an individual is a member. (5) There is a rather low concordance rate amongst monozygotic twins. (6) There is an increased risk of defect with increasing maternal age.

Neel believes that points (1) to (4) indicate the presence of complex genetic mechanisms underlying these defects, although points (5) and (6) indicate that environmental factors can influence the final expression of such mechanisms. Although a number of genetic mechanisms are known which might explain these observations, Neel himself favours the theory of genetic homeostasis. According to this theory, a population is most "fit" (in the evolutionary sense) when it maintains a certain level of heterozygosity. Individuals who do not have this minimum level of heterozygosity are defective and therefore cast off from the population. In other words, the malformed individuals are the price the population pays for its vigour. Neel suggested several ways by which this hypothesis could be tested.

Professor Turpin (Paris) discussed the amazing advances that have taken place during the past 1½ years in the field of human cytogenetics, and reviewed the rapidly increasing number of abnormalities now known to result from chromosomal excesses (e.g. mongolism; Klinefelter's syndrome; congenital heart disease and mental retardation; cleft lip and palate with microphthalmia); deficiencies (e.g. Turner's syndrome); and rearrangements (e.g. some cases of mongolism, polydyspondylia, etc.)

Professor Nachtsheim (Berlin) discussed interaction mechanisms between genes and environment in development, using a number of examples from his own work. For instance, an hereditary cataract in rabbits can be greatly modified by reducing the animal's water intake. A similar cataract can be induced in genetically normal animals by x-radiation, but albino animals are much more resistant to this effect of irradiation than pigmented ones. Thus, the genotype affects the response to an environmental agent, and vice versa.

Dr. Court-Brown (Edinburgh), in an extremely interesting paper, discussed the wide range of chromosomal sex variants which have been discovered to date, the time in development when these aberrations arose, the mechanisms underlying them and their impact on our understanding of sexual differentiation. In view of the fairly high incidence of these chromosomal abnormalities, Dr. Court-Brown felt that chromosomal studies should be done as a routine diagnostic test, particularly in cases involving sex anomalies and mental retardation.

In discussing this paper Dr. Book (Uppsala) seconded Dr. Court-Brown's final remarks. He pointed out that at present the chromosomes of approximately 1000 individuals in the world had been examined in detail. There are 25 separate conditions now known to result from chromosomal disturbances, and half of these concern sex anomalies. Obviously we have a great deal to learn about human cytogenetics, and future studies should be most profitable. However, several speakers warned of the considerable difficulties involved in such studies. It is certainly no coincidence that the major contributions to our knowledge to date in this field have been made by individuals who are animal and plant cytologists by training (Tjio and Levan, Chu, Ford, and Jacobs).

*Extrinsic Factors (Environmental)*

Dr. Josef Warkany (Cincinnati), whose experiments in the early 1940's on the experimental production of malformations in mammals initiated a new phase of teratology, presented an excellent review of environmental teratogenic factors.

Dr. Rhodes (Toronto) discussed the role of virus infection in human congenital malformations. Most of our knowledge in this field comes from the examination of the offspring of women who have contracted rubella during the first months of pregnancy. Although considerable data are now available regarding risk figures (perhaps as high as 50% if infection occurs in the first four weeks of pregnancy) and the types of defects encountered, there is no information regarding the mode of action of the virus. No one has been able to grow the virus in chick eggs or tissue culture, it cannot be transmitted to animals, and there is no simple laboratory diagnostic test. In discussing other viruses, Dr. Rhodes mentioned the current controversy regarding the teratogenic action of the Asian influenza virus. A study undertaken by Coffey *et al.* in Dublin seems to indicate that this virus is responsible for an increased incidence of anencephalic monsters. However, two studies from the United States did not show a significant increase. In closing, Dr. Rhodes referred to the lack of reliable data on virus-induced defects in animals. The information that is available indicates that attenuated forms of the hog cholera and blue tongue virus can be teratogenic, and Rhodes felt that these results dictate extreme caution in the use of attenuated poliovirus for the immunization of pregnant women.

Dr. Landauer (Connecticut) reviewed his outstanding work on induced defects which mimic spontaneously occurring anomalies (phenocopies). These studies raise many problems about the meaningfulness of making a sharp dichotomy between "genetic" and "environmental" causes of malformation.

In the discussion Dr. James Walker (St. Andrew's) touched upon this point when he stated that the association of increased incidence of anencephaly with decreasing social class might just as well result from genetic differences between classes as from environmental differences. He also mentioned that the few data available on racial variation with respect to this anomaly seem to be at odds with the association with social class reported by McKeown. In South Africa the incidence of anencephaly is lower in the native population than in the white population.

*General Developmental Mechanisms*

Dr. Edgar Zwilling (Brandeis University) spoke about "inductive mechanisms", using, as an example, an ingenious analysis of the development of the chick embryonic limb employing grafting procedures and the mutant gene for winglessness. The results demonstrate that the proper development of the wing depends upon an integrated reciprocal reaction between the ectodermal ridge tissue and the wing mesoderm. Zwilling stressed that this is not an exceptional finding and there are a great many similar situations known in developmental systems. The interaction of tissues can involve a number of mechanisms (e.g. simple physical contact, diffusible substances, or interactions between intercellular matrices), and Zwilling pointed out how

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disturbances of these inductive mechanisms could result in a wide range of anomalies.

Dr. Markert (Johns Hopkins University) gave an outstanding review of current knowledge on "Nucleocytoplasmic interactions during development". He began by discussing the perplexing problem of the role of gene action in differentiation. If all somatic cells contain the same gene complement, how can gene action account for the differentiation of various tissue types? From our knowledge of gene action in experimental animals we know that certain mutant genes do act specifically to alter developmental processes. In normal developmental processes such as pigment production, it is obvious that genes, present in all body cells throughout all stages of development, only produce their effect in specific cells at specific times. On the basis of such information it has been suggested that nuclei themselves undergo differentiation. This hypothesis has recently been confirmed by a series of elegant experiments on amphibia involving transplantation of nuclei during various stages of development to enucleated eggs and observing their subsequent development. The question still remains, "What turns genes 'off and on' at specific stages during development?" Although this question is far from being answered, a number of recent advances in the understanding of the molecular nature of gene action and of the ultramicroscopic structure of the cell have given extremely promising leads. Markert concluded by proposing a concept of progressively oscillating interactions between cytoplasm and chromosomes that should be a useful basis for further progress in this direction.

*Abnormal Developmental Mechanisms*

The moderator of this session, Dr. Paul Weiss (Rockefeller Institute), pointed out that the only division between it and the previous one involved a lunch-hour break, that there was no sharp boundary between normal and abnormal development, and that any attempts to establish such a boundary were artificial and unrealistic.

Dr. Fraser (McGill University) presented a paper on "The use of teratogens in the analysis of abnormal developmental mechanisms", in which he pointed out that teratogens can now be used in the same manner as mutant genes to investigate where and how the developmental deviations leading to congenital defects go wrong. By studying the effects of antimetabolites and specific inhibitors on animals of various genotypes it should be possible to clarify the metabolic requirements of various organogenetic processes, and come to a better understanding of the biochemical bases of developmental errors.

Dr. James G. Wilson (Gainesville), speaking on "General principles in experimental teratology", enunciated five principles and illustrated each with examples. (1) The embryologic stage at the time when an agent acts determines which tissues are susceptible to teratogenesis. (2) Teratogenic agents interfere with particular phases of metabolism, which often produces characteristic patterns of malformations. (3) Teratogenic agents often, if not always, act in a complementary fashion with the genotype of the embryo to produce malformations. (4) Intrauterine mortality tends to vary directly with the rate of malformations. (5) An agent which is very damaging to the embryo may be relatively harmless to the mother.

In the final paper, Dr. Wolff (Collège de France) discussed "Fetal hormones and morphogenesis". Most of the endocrine glands begin to function after the critical stages of differentiation and organogenesis have passed, and the impact of most hormones on these phases of development is negligible. However, the sex hormones are an exception to this rule, and Dr. Wolff discussed some of the experiments involving gonadal transplantation and parabiosis in amphibians which have given information regarding the factors responsible for the normal development of sex.

*Maternal-Fetal Interactions*

Dr. Anne McLaren (Edinburgh), speaking on "Maternal effects in mammals and their experimental analysis", divided these effects into three major classes: (1) *Cytoplasmic* — occurring before fertilization; (2) *Uterine*—(a) occurring before fertilization and involving the environment of the oviduct and uterus; (b) occurring after fertilization; (3) *Milk*—occurring postnatally and involving factors associated with the colostrum and milk. Dr. McLaren then discussed techniques employed for differentiating these effects, using investigations on the mouse and rabbit as examples. These techniques include foster nursing, whole embryo transfer, transfer of unfertilized eggs, and ovarian transplantation.

Dr. Hemmings (Bangor, Wales) discussed the transfer of antibody from mother to fetus, which appears to be a matter of active cellular transport by yolk-sac endoderm in some species, of allanto-chorionic placenta in others (presumably including man). The endodermal cells appear to be highly selective in the type of molecule transferred. Dr. Thomas (New York) described evidence that syncytial trophoblasts normally enter the maternal blood stream and discussed the possible immunological significance of this phenomenon.

Although these papers were not concerned with abnormal development, they were important because they stressed the fact that the placenta can no longer be considered as an impassable barrier separating the fetal and maternal organisms.

*Physiological and Medical Problems*

Dr. Barron (Yale University) discussed some of his experiments on the "Homeostasis of the fetus". Studying pregnant ewes at high altitudes, he was able to show that regardless of fluctuations in the oxygen tension of the maternal blood, the oxygen tension of fetal blood remained remarkably constant at a relatively low level. The placenta seems to play the role of homeostatic regulator. These findings suggest that malformations produced by exposing pregnant animals to hypoxia are not a result of fetal hypoxia. If the existence of such a fetal homeostatis could be confirmed, it would be interesting to know when it comes into existence.

Dr. McKay (Boston) discussed the work of Drs. Hertig and Rock on the very early development of human embryos, obtained from women who were about to have a hysterectomy and had arranged the last coitus before operation at a time that would assure an optimal probability of successful fertilization. Thirty-four of 107 uteri were found to have fertilized ova, ranging from the two-cell stage to early implantation of a 17-day villous ovum. Of these 34 zygotes, 24

were normal and 10 were abnormal. Dr. McKay discussed some of the anomalies found and outlined the multitude of difficulties in such a study.

Dr. James Walker (St. Andrew's) discussed "Anencephaly in Scotland". This study involved a survey of all anencephalic births in Dundee from 1950 to 1959. The findings indicate that this area of Scotland has one of the highest incidences of this defect in the world (about 3/100 births). Some of the findings confirmed, while others did not support, the work of McKeown (*op. cit.*). There appeared to be a secular variation, as McKeown reported. Seasonal variation was also present, but showed a different pattern from 1950 to 1954 than from 1955 to 1959. Is this statistical fluctuation or a result of changing environmental patterns? There was no clearcut maternal age effect or a significant variation with respect to social class. The sex ratio was eight females to three males. Dr. Walker suggests that the form of anencephaly occurring in males is less severe and does not involve the whole vertebral column. Dr. Potter (Chicago), in discussing this paper, corroborated this point.

The final paper of this session was by Dr. James L. Wilson (Michigan), on "Congenital anomalies in modern clinical medicine". Dr. Wilson, after reviewing the rapid progress in methods of treatment, discussed the tremendous impact congenital defects have on the individual, the family and society. Even those defects which surgical procedures have removed from the lethal list (e.g. harelip and cleft palate) present considerable problems. For example, the child with a severe cleft palate may face many years of speech therapy and orthodontic treatment after the defect has been repaired. If this therapy does not progress favourably, psychological and social problems may complicate the picture. The complications in cases of spina bifida are even more severe. A child with such a defect is often confined to a wheelchair or is forced to use crutches and braces for life. In addition, there may be partial or complete incontinence of bladder and/or bowel. Such children, often with normal intelligence, usually experience emotional difficulties associated with their restricted existence. Problems may also arise from the fact that each aspect of the medical problem may be treated by a separate specialist, with no one guiding the overall program over the years, and assuring proper follow-through of the rehabilitation program. Dr. Wilson felt that this chronic aspect of the problem of congenital defects had not been recognized sufficiently by the medical profession, and he appealed for a better awareness of the considerable psychological and social implications of the more severe forms of abnormalities.

### *Perspectives*

The first paper of the final session was presented by Professor C. H. Waddington (Edinburgh) on "Genetic control of the stability of development". Professor Waddington pointed out that a developing system has tremendous regulatory potentiality. The regulatory mechanisms exist, presumably, as an outcome of natural selection. There are periods, however, when the developmental stability is low (Waddington has termed them periods of "epigenetic crises"). For example, in amphibia the time of gastrulation, when cell movements are at a maximum and many inductive processes are taking place, is a critical period. It is usually during this critical period that teratogenic agents produce their most severe effects. Each species has similar critical periods. Studies in the genetics of reaction to teratogenic agents illustrate the great diversity of genetic mechanisms controlling the stability of development.

Dr. E. L. Tatum (Rockefeller Institute), in a paper on "Some molecular aspects of congenital malformations", gave a résumé of our present knowledge of the nature of the genic material and its role in controlling protein synthesis. Dr. Tatum reviewed the recent dramatic advances in our knowledge of the relation between gene structure and protein specificity, and considered some of the ways in which gene activity might be selectively controlled during differentiation, including induction, suppression or regulation of enzyme activity. Progress in this field could lead to therapeutic measures in those defects resulting from genetic abnormalities. Eventually it might even be possible to alter the gene in a controlled way in higher organisms as it can now be done in bacteria by DNA transformation—"the ultimate in biological engineering".

In a paper entitled "Future possibilities in the genetical study of congenital malformations," Professor L. S. Penrose (London) stressed that our precise knowledge of genetical mechanisms now known to be responsible for certain congenital defects is extremely limited. There are many genetical mechanisms known in lower animals which might exist in man and be significant in our understanding of malformation (see Neel's theory, *op. cit.*).

Dr. Ebert (Carnegie Institution of Washington), in a provocative paper entitled "Antibodies, viruses, and embryos", discussed some of the ways that viruses have been and could be used to investigate the mechanisms by which information is carried between the genes and the rest of the cell, and how cell specificity develops. In considering the teratogenic effects of viruses he emphasized the point made by Professor Waddington that a critical stage of development is usually one during which there is considerable movement of cell groups and interaction of different cell types. The specificity of cell surfaces involved in these processes is probably of critical importance, and Ebert suggests that virus particles introduced into the embryo may produce their teratological effects by altering surface specificity. The possibility that immunological mechanisms might be involved was also stressed.

### CONCLUSION

As may be judged from this report, the First International Conference on Congenital Malformations was very comprehensive in its approach. The conference was intended to be a general review of the whole field, and a majority of the speakers adhered to review presentations nicely spiced with current investigations. The decision to have a review type of program was a wise one for a first conference of this nature, and the published proceedings should be an excellent source book which outlines the present knowledge, gaps in knowledge, and the prospects for future research into the causes of malformations.

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# GENERAL PRACTICE

## SEVENTH ANNUAL CLINICAL MEETING, COLLEGE OF GENERAL PRACTICE OF CANADA (ALBERTA CHAPTER) AND SECTION OF GENERAL PRACTICE, C.M.A. ALBERTA DIVISION

THE SEVENTH Annual Clinical Meeting of the College of General Practice of Canada (Alberta Chapter) and the Section of General Practice, Alberta Division, C.M.A., will be held in Banff, Alta., on January 25, 26 and 27, 1961. The Mount Royal Hotel will be convention headquarters. All scientific and business meetings will be held in the Cascade Hall. This meeting is rated at 15 hours of Formal Study Credits. The program is as follows:

*Wednesday, January 25*

Morning Session (Chairman, Dr. J. J. Dobry): "Hints to Make Obstetrics Easier"—Dr. D. R. Buchanan; "Some New and Interesting Concepts in the Field of Allergy"—Dr. T. H. Aaron; "Acute Rheumatic Fever"—Dr. N. F. Duncan; "Modern Aids in the Diagnosis of Anemia"—Prof. D. G. Cameron.

Afternoon Session (Chairman, Dr. A. Murray): "Your Patient at the Cancer Clinic"—Dr. A. B. McCarten; "Common Foot Disabilities in Children and Adults"—Dr. O. Rostrup; "An Evaluation of Surgical Measures in the Treatment of Patients with Strokes"—Dr. P. E. Bernatz; "Some Aspects of the Problem of Hyperparathyroidism"—Dr. R. E. Hatfield.

*Thursday, January 26*

Morning Session (Chairman, Dr. J. A. Weddell): "Anticoagulant Therapy"—Drs. G. J. Bell, D. M. Bell and H. E. Bell; National Research Council (speaker to be announced); "The Challenge of the Inguinal Hernia"—Dr. P. E. Bernatz.

Afternoon Session (Chairman, Dr. P. B. Rose): "Clinical Diagnosis and Modern Concepts of Malabsorption"—Prof. D. G. Cameron; Meeting of the College of General Practice, Alberta Division; Meeting of the Section of General Practice, Alberta Division, C.M.A.

*Friday, January 27*

Morning Session (Chairman, Dr. J. Moriarty): "Intestinal Obstruction in Infancy"—Dr. D. N. Ramsay; "Interesting Eye Problems in General Practice"—Dr. D. L. Rees; "So Your Cholesterol Level is High!"—Dr. D. G. Cameron; "The General Practitioner's Psychiatric Care of the Child"—Dr. A. R. Schragg.

Afternoon Session (Chairman, Dr. A. M. Leacock): "The Social Problem of the Central European Immigrant"—Dr. Julius Guild; "The Radiological Interpretation of the Scout Film in the Acute Abdomen"—Dr. H. E. Duggan; "Diaphragmatic Hernia—A Medical or Surgical Problem?"—Dr. P. E. Bernatz; General Practice Workshop, with Dr. J. Smulski as Moderator and Drs. D. N. Ramsay, D. L. Rees, A. R. Schragg, J. Guild and H. E. Duggan.

Luncheons will be held on each of the days. The Hon. J. D. Ross, M.D., Minister of Health for the Province of Alberta, will be the speaker at the luncheon on Monday, January 25; Dr. W. V. Johnston, Executive Director of the College of General Practice of Canada, on Tuesday, January 26; and Dr. A. R. Schragg, on Wednesday, January 27. The annual reception, banquet and dance will take place on Friday evening. A special program has been planned for the ladies.

Further information about the meeting may be obtained from Dr. E. R. Haynes, Secretary, Alberta Chapter, 10951-124th St., Edmonton, Alta.

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## ERRATUM: GENERAL PRACTICE RESIDENCIES

In the list of general practice residencies in Canada (Section of General Practice, *Canad. M. A. J.*, 83: 1282, December 10, 1960) it was incorrectly stated that Dr. A. J. Brunet was Medical Director of the Misericordia Hospital in Edmonton, Alta. Dr. G. R. Macdonald is Medical Director of this hospital.

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## LE BLUFF AMERICAIN

(Reprinted from the *Canadian Medical Association Journal*, 1: 32, 1911.)

En mars 1909, un certain médecin américain, du nom de Flexner,—Abraham, de son petit nom—est venu à Montréal dans le but d'étudier le fonctionnement des universitiés Laval et McGill et faire rapport au nom d'une institution philantropique américaine designée sous le nom de 'fondation Carnegie'.

Son rapport sur l'école de Médecine Laval, a Montréal, est très défavorable. Malheureusement pour la fondation Carnegie et aussi pour nous, à l'étranger, tout est faux dans ce rapport: chiffres, dates, salaires, enseignement théorique et pratique, etc. C'est une infamie.

Son rapport sur McGill est très élogieux. Cela se comprend; affinites de races, belles batisses, riches dotations. L'américain, bluffeur, avant tout, se laisse facilement impressionner par ce qui frappe la vue: marbres imposants, colonnes dorées. C'est, du reste, sa seule façon à lui, d'impressionner l'étranger.—*L'Union Médicale du Canada*, December 1910.

# PUBLIC HEALTH

## SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

### PARALYTIC POLIOMYELITIS

*Canada*

A total of 52 cases of paralytic poliomyelitis was reported to the Epidemiology Division during the last two weeks. Eighteen cases were reported in the 44th week ended November 5 and 34 in the 45th week ended November 12. This brings the 1960 cumulative total to 748 cases. The increase in the number of cases reported in the 45th week appears to be mainly due to delayed reports.

According to preliminary figures on the dates of onset, it would appear that in all provinces where high reporting was registered, the peaks were reached during the last week of August and first two weeks of September.

Reports on virus isolations have been received from several provinces. An increase in the number of poliovirus type III recoveries is noted across Canada, and especially in the province of Quebec, where the epidemic strain was type III while type I was isolated only in sporadic cases.

The table below summarizes reports received to date.

| | *Nfld.* | *Que.* | *Ont.* | *Man.* | *Alta.* | *B.C.* | *Total* |
|---|---|---|---|---|---|---|---|
| Total poliovirus isolations | 6 | 43 | 16 | 8 | 59 | 40 | 172 |
| Poliovirus type I | 6 | 11 | 13 | 4 | 53 | 34 | 121 |
| Poliovirus type III | — | 31 | 3 | 4 | 6 | 6 | 50 |
| Poliovirus type II | — | 1 | — | — | — | — | 1 |

Among the aseptic meningitis isolations, Coxsackie B2 is prevalent in the province of Quebec, especially in the Montreal region. In British Columbia, there was a high incidence of Coxsackie B5 infections during the summer months.

### PERICARDITIS DUE TO COXSACKIE VIRUS

A case of pericarditis due to Coxsackie virus B5 has been reported from Calgary, Alta. The patient had fever, cervical adenitis and sore throat. On examination, pericarditis was also present. Stools were submitted for virus studies, and Coxsackie virus B5 was isolated. There were no meningeal symptoms. The patient made a complete clinical recovery.

### FOOD POISONING

An outbreak of food poisoning occurred at a school in Haney, British Columbia, affecting about 20 to 30 teachers. The symptoms were nausea, vomiting, abdominal pains and diarrhea. No information is as yet available on the source or cause of the outbreak.

### TRICHINOSIS

Two more cases of trichinosis were reported from Vancouver for the week ended November 5, 1960. Five cases were reported in the previous week.

### TULAREMIA

One case of tularemia has been reported in Ontario for the week ended October 29. This is the fifth case reported from Ontario during 1960.

*Indian and Northern Health Services*

The following reports have been received from the Director, Indian and Northern Health Services, Ottawa:

A second case of diphtheria has been reported from the Keeseekoowenin Indian Reserve at Elphinstone, Man. This is a contact of a case previously reported. Antitoxin is being administered to all the contacts.

An outbreak of whooping cough has been reported from a settlement at Grise Fiord, N.W.T., with a population of 60 Eskimos and two R.C.M.P. officers. Six children under 5 years of age developed whooping cough complicated by bronchopneumonia. There was one death, in a 7-month-old baby. The R.C.M.P. initiated treatment with antibiotics. Dr. A. H. Stevens (I.N.H.S.) left Ottawa on November 5 to investigate the outbreak. He reported that by November 12, the situation appeared under control. The older children and the rest of the population have had yearly inoculations of pertussis vaccine. The most likely source of infection was the visit of the Eastern Arctic Patrol vessel in late September 1960.

An outbreak of dysentery due to *Shigella flexneri* has been reported from the Joseph Bighead Reserve at Goodsoil, Sask. One death has been reported.

### TROPICAL DISEASES

*Canada*

Further to the report from the Department of Veterans Affairs on tropical diseases diagnosed on personnel returning

PARALYTIC POLIOMYELITIS IN CANADA*
45TH WEEK—ENDING NOVEMBER 12, 1960

| | *Reported cases* | | | | | | | | | *Deaths* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *This week* | | | *Last week* | | | *To this date* | | | *To this date* | | |
| | *1960* | *1959* | *1958* | *1960* | *1959* | *1958* | *1960* | *1959* | *1958* | *1960* | *1959* | *1958* |
| Canada | 34 | 35 | 1 | 18 | 39 | 5 | 748 | 1785 | 232 | 67 | 169 | 22 |
| Newfoundland | 1 | 1 | — | 1 | 1 | — | 46 | 135 | 4 | 4 | 12 | — |
| Prince Edward Island | — | — | — | — | — | — | 1 | 7 | — | — | 1 | — |
| Nova Scotia | — | — | — | — | 1 | — | 9 | 7 | — | 1 | — | — |
| New Brunswick | 1 | 3 | — | — | 1 | — | 50 | 56 | 4 | 2 | 6 | 1 |
| Quebec | 15 | 13 | 1 | 7 | 17 | 4 | 211 | 1127 | 73 | 30 | 100 | 2 |
| Ontario | 3 | 2 | — | 3 | 3 | — | 35 | 195 | 18 | 1 | 20 | 5 |
| Manitoba | 1 | — | — | — | — | 1 | 12 | 26 | 101 | 1 | 2 | 10 |
| Saskatchewan | 4 | — | — | — | 2 | — | 49 | 41 | 1 | 8 | 3 | — |
| Alberta | 5 | 3 | — | 6 | 3 | — | 174 | 65 | 21 | 8 | 10 | 1 |
| British Columbia | 4 | 13 | — | 1 | 11 | — | 160 | 115 | 9 | 12 | 11 | 3 |
| Yukon | — | — | — | — | — | — | — | — | — | — | 4 | — |
| Northwest Territories | — | — | — | — | — | — | 1 | 11 | 1 | — | — | — |

*Weekly returns based on telegraphic reports by provinces.

| | 1955 | 1956 | 1957 | 1958 | 1959 | 1960 | Total findings |
|---|---|---|---|---|---|---|---|
| *Giardia lamblia* | 6 | 13 | 8 | 13 | 5 | 3 | 48 |
| *Trichuris trichiura* | 3 | 12 | 8 | 5 | 1 | 2 | 31 |
| *Endamoeba histolytica* | 12 | 19 | — | 6 | 3 | 1 | 41 |
| *Endamoeba nana* | 1 | — | — | — | 1 | — | 2 |
| *E. vermicularis* | — | — | — | 1 | — | — | 1 |
| *Endamoeba coli* | — | 2 | 5 | 4 | 1 | — | 12 |
| Amebic hepatitis | — | — | — | 1 | — | — | 1 |
| Amebiasis | — | — | — | — | — | 2 | 2 |
| *Ascaris lumbricoides* | 2 | 2 | 2 | — | 1 | 1 | 8 |
| *Taenia saginata* | — | 1 | — | 1 | — | — | 2 |
| *Iodamoeba butschlii* | 2 | — | 2 | — | — | — | 4 |
| Whipworm | — | 1 | 1 | 1 | — | — | 3 |
| Trichinosis | — | — | — | 1 | — | — | 1 |
| Charcot-Leyden crystals | — | — | — | — | 1 | — | 1 |
| Shigella | 1 | 1 | — | — | — | — | 2 |
| Salmonella | — | — | 1 | 1 | — | — | 2 |
| Multiple infections | — | 1 | 2 | 2 | 6 | — | 11 |
| Negative findings | 47 | 153 | 100 | 95 | 66 | 43 | 504 |
| Total examined | 74 | 205 | 129 | 131 | 85 | 52 | 676 |
| Percentage positive | 36.5 | 25.3 | 22.5 | 27.5 | 22.3 | 17.3 | 25.5 |

from overseas (Surveillance Report of October 8, 1960), the following information has been received from the Department of National Defence, Office of the Surgeon-General, Canadian Forces.

Since 1955, all service personnel returning from Indo-China, after service with the United Nations Truce Commission, have been investigated for parasitological infection, immediately on their return to Canada. Surveillance and follow-up of all positive cases were maintained by the Medical Services, and after initial treatment, all patients were followed up until free of parasitological or bacterial infection.

The accompanying table summarizes the findings for the period 1955 to 1960.

## RABIES

### *United States*

The Ohio "Animal Disease Trends" for September states that the eighth case of rabies in bats in Ohio was confirmed on September 27, 1960. The bat was found alive, but unable to fly, in a schoolyard by school boys who captured it as a matter of curiosity. The following day the incident was called to the attention of the school and local health authorities, who submitted the bat to the State Health Department Laboratory. No scratches or bites were observed on the two boys. Fluorescent antibody and mouse inoculation tests on the bat brain tissue were positive for rabies. Both boys were started on a series of antirabies vaccine injections.

Epidemiology Division, Department of
National Health and Welfare.
Ottawa, November 19, 1960.

## SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

| *Disease* | *Week ended (1960):* Nov. 12 | Nov. 19 | Nov. 26 | Dec. 3 | *Cumulative total since beginning of year* 1960 | 1959 |
|---|---|---|---|---|---|---|
| Brucellosis (Undulant fever) (044) | 2 | 1 | 2 | 1 | 126 | 107 |
| Diarrhea of the newborn, epidemic (764) | 1 | — | — | 1 | 45 | 82 |
| Diphtheria (055) | 6 | — | 3 | 2 | 43 | 33 |
| Dysentery: (045, 046, 048) | 244 | 39 | 29 | 29 | 2,811 | 1,257 |
| (a) Amebic (046) | — | 1 | — | — | 3 | 2 |
| (b) Bacillary (045) | 105 | 28 | 19 | 28 | 2,221 | 1,098 |
| (c) Other and unspecified (047, 048) | 139 | 10 | 10 | 1 | 587 | 157 |
| Encephalitis, infectious (082.0) | — | — | 1 | 1 | 9 | 21 |
| Food poisoning: (049.0, 042.1, 049.2) | 54 | 13 | 18 | 22 | 1,162 | 784 |
| (a) Staphylococcus intoxication (049.0) | — | — | — | — | 309 | 17 |
| (b) Salmonella with food as vehicle of infection (042.1) | 19 | 11 | 17 | 22 | 778 | 621 |
| (c) Unspecified (049.2) | 35 | 2 | 1 | — | 75 | 146 |
| Hepatitis, infectious (including serum hepatitis) (092, N998.5) | 191 | 164 | 186 | 167 | 5,450 | 4,286 |
| Meningitis, viral or aseptic (080.2, 082.1) | 6 | 1 | 10 | 8 | 578 | 888 |
| Meningococcal infections (057) | — | 1 | 1 | 1 | 143 | 188 |
| Pemphigus neonatorum (Impetigo of the newborn) (766) | — | — | — | — | 7 | 4 |
| Pertussis (Whooping cough) (056) | 119 | 154 | 93 | 130 | 5,548 | 6,609 |
| Poliomyelitis, paralytic (080.0, 080.1) | 31 | 14 | 16 | 16 | 799 | 1,816 |
| Scarlet fever and Streptococcal sore throat (050, 051) | 299 | 253 | 270 | 359 | 19,655 | 20,307 |
| Tuberculosis:‡ (001-019) | 101 | 99 | 115 | 129 | 5,696 | 5,948 |
| (a) Pulmonary§ (001, 002) | 74 | 77 | 85 | 115 | 4,441 | 4,654 |
| (b) Other and unspecified§ (003-019) | 6 | 13 | 7 | 7 | 539 | 471 |
| Typhoid and Paratyphoid fever (040, 041) | 8 | 4 | 3 | 10 | 314 | 538 |
| Venereal diseases: (020-039) | 299 | 371 | 443 | 340 | 16,504 | 15,764 |
| (a) Gonorrhea (030-035) | 255 | 318 | 399 | 301 | 14,599 | 13,759 |
| (b) Syphilis (020-029) | 44 | 53 | 44 | 38 | 1,900 | 1,997 |
| (c) Other† (036-039) | — | — | — | 1 | 5 | 8 |

*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
†Including chancroid, granuloma inguinale and lymphogranuloma venereum.
‡Newfoundland and Nova Scotia data included in cumulative totals only.
§Ontario data excluded.

# OBITUARIES

DR. W. C. ARNOLD, aged 78, died December 7 in hospital in London, Ont. A graduate of the University of Toronto in 1903, he held the rank of colonel and organized overseas medical services during World Wars I and II.

DR. ONESIME BEDARD, aged 54, died November 10 in Ottawa. A graduate in medicine from Laval University in 1931, he practised in Quebec and latterly in Ottawa for 25 years.

Dr. Bédard is survived by his widow, three sons and four daughters.

DR. ROBERT N. BURNS, 83, died in Winnipeg on November 25. Born in Burford, Ont., he moved to Winnipeg in 1883. He was educated in the schools of that city and graduated in arts from Manitoba College and in medicine from Manitoba Medical College in 1905. His internship was spent in St. Boniface Hospital, and he began private practice in 1908. During his student days he played on several championship soccer teams.

Dr. Burns is survived by a sister. R.M.

DR. PHILLIPPE CHABOT, aged 64, died November 14 at his home in Ville-Marie, Que., where he had practised medicine for the past 35 years. Dr. Chabot was known in the Temiskaming district as "The Doctor of the Poor" as a result of the many years he served the community. He was mayor of Ville-Marie for 17 years.

DR. WILLIAM A. CHESTNUT, 79, of Moosomin, Sask., died on November 15. He will be remembered by many of the older graduates of Manitoba Medical College, from which he graduated in 1913. He practised in Teulon, Transcona, Tyndall and Minto before moving in 1919 to Moosomin, where he played an active part in community affairs.

Dr. Chestnut is survived by his widow, three sons, one of whom is Dr. Harold W. Chestnut of Moosomin, and two daughters. R.M.

DR. ARTHUR FREDERICK DUNN, aged 63, died November 7 at his home in Ottawa. After graduating from McGill University in 1930, he practised in Ottawa.

Surviving are his widow, two sons and two daughters.

DR. FRANCIS LOUIS EBERHART, aged 74, died in Meaford General Hospital on November 4. A graduate of the University of Toronto in 1914, Dr. Eberhart practised in Meaford for 43 years until his retirement 15 months ago.

He is survived by his widow and one daughter.

DR. J. EMMANUEL GAGNE, aged 80, died November 19 in Montreal. A graduate of Laval University in 1904, he served as medical officer of the Montreal Police Department for more than 30 years.

He is survived by two sons and two daughters.

# BOOK REVIEWS

**ROSE AND CARLESS MANUAL OF SURGERY. Consulting Editor, Sir Cecil Wakeley, Bt., K.B.E., C.B. Edited by Michael Harmer and Selwyn Taylor, assisted by 15 contributors. 19th ed. 1389 pp. Illust. Baillière, Tindall & Cox, London, 1960. $14.25.**

For the past 60 years, undergraduate students as well as graduates studying for their Fellowship have made use of this book in their studies. It has generally been considered to contain more information than any comparable textbook in surgery.

It is a particularly comprehensive book, as it has been in the past. It is different from most general surgical textbooks in that it includes sections on ophthalmology, otolaryngology, gynecology and tropical surgery.

The present edition has been published in one volume and this has many obvious advantages. The deletion of the chapter on anesthesia will not detract from it, inasmuch as there are now many textbooks in anesthesia which may be consulted. Another pleasing feature has been the incorporation of brief biographies of the two original authors. This will meet with the approval of those who have an interest in the history of surgery.

The first chapter deals with the general principles related to infection, shock, electrolyte disturbances, wounds, burns, chemotherapy, blood transfusions and other topics. It has been brought completely up to date with the latest information concerning advances in the care of the surgical patient.

Subsequent chapters are devoted to the surgery of the different organs and systems. Each subject is dealt with in an orderly fashion, first outlining the pathology or altered anatomy, signs and symptoms, diagnosis and treatment. Detailed discussion of the techniques of operations is not provided but the general principles are outlined.

It is a great tribute to any book that it is still in use 60 years after publication of the first edition. With this new edition, Rose and Carless will be assured of a permanent place in all medical libraries and reading rooms. It is one of the most up-to-date and complete works in surgery. It will be particularly helpful to medical students, practising surgeons and any who wish to consult an excellent surgical textbook.

**GYNECOLOGICAL UROLOGY. Edited by Abdul Fattah Youssef. 826 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $24.75.**

Dr. Youssef has successfully welded two important subjects into one for the first time by providing a manual on gynecological urology which will be of great benefit to both practising gynecologists and urologists. The contributions from 31 eminent men from eight countries perhaps may be old hat to people who are acquainted with their works, but to students, residents, and indeed practising urologists and gynecologists, it is an excellent and comprehensive form of reference.

It is well put together, and the contributions are short, concise and to the point. It is a pleasure to review this type of book.

Canad. M. A. J.
Jan. 7, 1961, vol. 84

**SYPHILIS: MODERN DIAGNOSIS AND MANAGEMENT. United States Public Health Service Publication No. 743. 58 pp. Illust. U.S. Government Printing Office, Washington, D.C., 1960. $2.00.**

This most recent publication on syphilis by the United States Department of Health, Education and Welfare is a useful book of 58 pages. It includes chapters on etiology, modern methods of diagnosis and treatment, the course and stages of the disease, and special problems encountered in the form of atypical signs and symptoms, weak serologic reactivity, biological false reactions and side effects of penicillin. These chapters, as well as the colour illustrations, present in concise form a wealth of practical knowledge of value in the diagnosis and management of the disease. This book is recommended for practising physicians as well as for those engaged in the field of public health.

**PAGES IN THE HISTORY OF CHEST SURGERY. Rudolph Nissen and Roger H. L. Wilson. 151 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $8.25.**

The twentieth century has presented many fascinating developments in thoracic surgery. Yet, in 1896, Stephen Paget wrote: "We have reached a point in this domain of our art [surgery of the chest] that we can hardly go beyond." Nissen and Wilson in their monograph have presented some of the interesting features in the enormous progress of thoracic and heart surgery in the last 75 years. Brief mention is made of the Canadian contributions of the hilus tourniquet of Shenstone and hypothermia by Bigelow.

Considerable space is given to the reproductions of pages of original articles and photographs of thoracic surgeons. In some of the reproductions the type is small and it is difficult to read.

This book is not written as a comprehensive history of thoracic surgery in the twentieth century, but discusses many of the interesting advances and contributions made in this period.

**CONTROLLED CLINICAL TRIALS. Papers delivered at the Conference Convened by The Council for International Organizations of Medical Sciences. Organized under the direction of Professor A. Bradford Hill. 177 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $6.00.**

Drug trials in man have in quality lagged far behind those in other biological fields, largely, perhaps, because the idea of "experimenting" on human subjects has been abhorrent to layman and physician alike. Yet the history of such drugs as dicoumarol, the value of which is still in dispute after 15 years of haphazard use, shows that in most instances, adequately controlled studies must sooner or later be undertaken.

Nobody has championed the cause of applying the discipline of statistics to clinical medicine more stoutly than Professor A. B. Hill, the master mind behind this book. The papers given at a conference under his chairmanship in Vienna in 1959 have been collected into this neat little volume. Although it contains nothing new in theory of experimental design, as a guide to the adaptation of the well-established pigs-and-corn type of study to clinical medicine, it is a revelation. The contributors, all seasoned workers in the field and most of them practising physicians, discuss the subject from many aspects. For example, Fletcher gives some chastening data on observer error; Witts and Atkins tackle the thorny ethical problems, if anything over-conscientiously. All show a lively insight into bias, inadequacies of planning and illogicality of decision, faults against which the most ingenious statistician is powerless. Pickering has some refreshingly sensible comments in summary: the chairman appropriately has both a prologue and an epilogue with much wisdom in both.

The papers contain numbers but no statistical analysis and this is on the whole wise, since nothing discourages the uninitiated so much as masses of exotic symbols. It is perhaps a pity that an exception was not made for sequential analysis (the uses of which are briefly discussed). It is likely to have an important future, and the method has not yet won a place in the standard elementary texts on statistics.

We are spared the other two sources of mystification now so common—ambiguity and obscurity of style—the papers being coherent and lucid, even if one or two of the diagrams are a little confusing.

To all engaged in drug trials this book should prove at least a useful introduction to method; certainly the clinical statistician has much practical information to glean from it. Even those whose interest is mainly to read the literature well will find their discernment sharpened by it, and it would not be out of place in the undergraduate medical curriculum.

All in all, this is an admirable little book.

**CLINICAL VECTORCARDIOGRAPHY AND ELECTROCARDIOGRAPHY. E. Massie and T. J. Walsh. 592 pp. Illust. Year Book Publishers, Inc., Chicago, Ill., 1960. $27.50.**

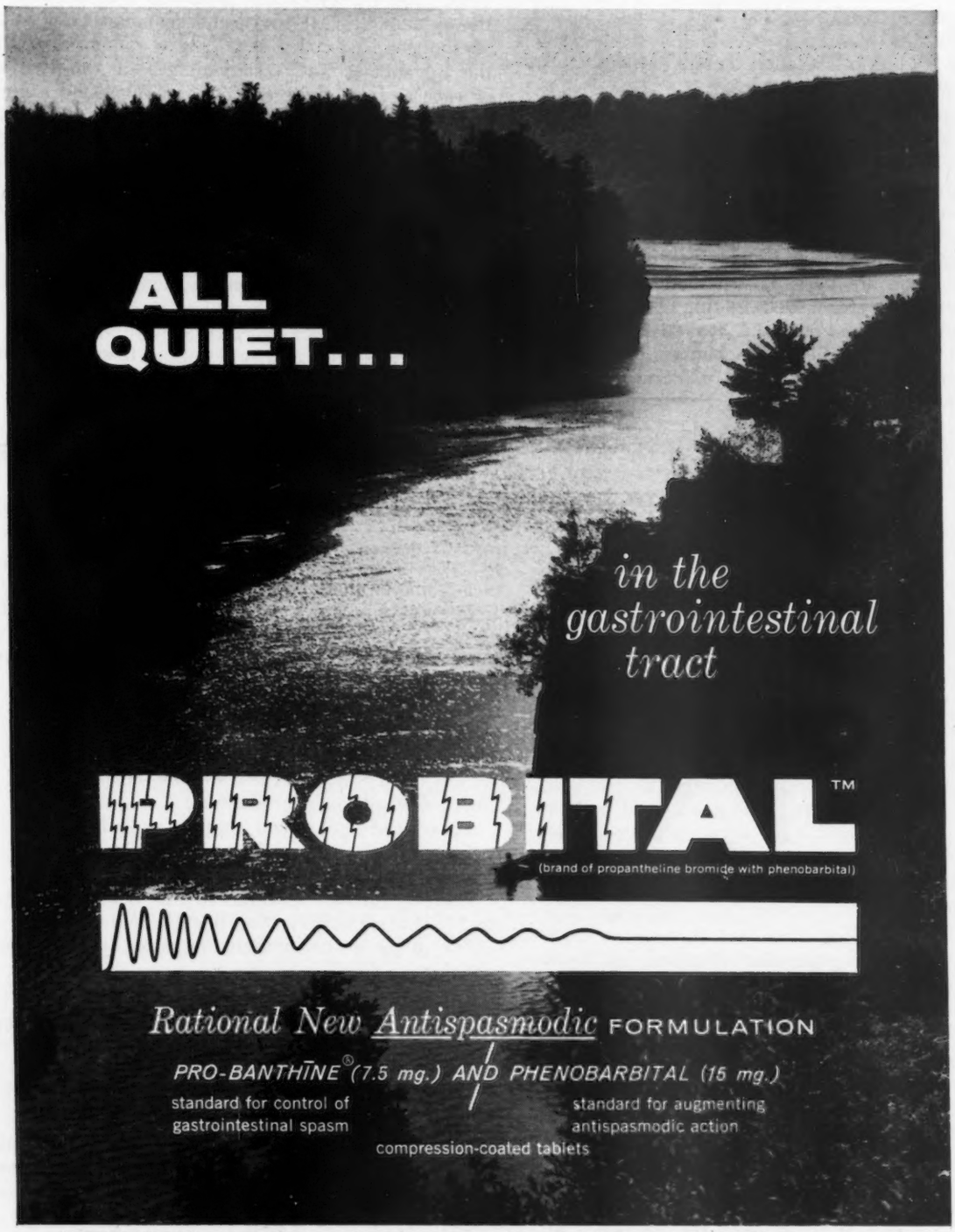
This comprehensive volume is timely in that it fills the gap which formerly existed when the postgraduate student sought instruction in vectorcardiography. Study of the latter has been rendered difficult by the lack of standardization of techniques, particularly in regard to electrode placement. In the resulting confusion many a student has become discouraged and decided to postpone the undertaking. Now, however, he may resume his efforts in the knowledge that, while many difficulties still remain, he will find the effort well worth his while.

The book takes the student through the basic considerations of the theory of electrical activity of myocardium and develops the standard normal ECG and VCG lead systems. The various waves or loops are concisely described and their genesis is explained by cleverly constructed diagrams of heart positions, electrical changes and simple mathematics. The reasons for commonly accepted terms, such as ventricular gradient and spatial QRS-T angle, are succinctly given and their value is stated.

There follow sections on ventricular hypertrophy, bundle branch block, myocardial infarctions, cardiac arrhythmias, and finally a section of "Illustrative Vectorcardiograms and Electrocardiograms".

Although the VCG's are all examples of the Grishman cube system of electrode placement, which may be somewhat less accurate than those done by the Frank system, the graduate student should find this book of great value both for initial knowledge and for later reference in this field.

*(Continued on page 70)*

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*(Continued from page 68)*

**THE BASIC PHYSICS OF RADIATION THERAPY. A New Book Presenting the Basic Physics. Joseph Selman. 646 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $16.00.**

This book is a clearly written and well-organized description of the basic physics which are necessary in the understanding of radiation therapy. It is liberally illustrated, with concise diagrams.

The author starts with the assumption that the reader has little knowledge of mathematics or physics, and explains in a simple and readable way the complicated concepts involved. The sections on pure radiation physics are excellent and include chapters on the nature of radiation, interactions between radiation and matter, x-ray production, and radioactivity. Some chapters on clinical application are perhaps superfluous in a book of this type and they rather lack the ring of authenticity which is evidenced elsewhere. An attractive feature is the frequent summarization of sections. There is a valuable appendix, in which useful physical data and equations are listed.

Errors are rare, but one such example, which recurs, is the apparent quantitative equation in the author's mind of L.E.T. and R.B.E.

This book can be recommended without qualification, to postgraduate students in radiation therapy and also to x-ray therapy technicians.

**EXPERT COMMITTEE ON POLIOMYELITIS, Third Report. WHO Technical Report Series No. 203. 53 pp. World Health Organization, Geneva, Switzerland, 1960. 60 cents. Also available in French and Spanish.**

Since the last WHO Expert Committee on Poliomyelitis met in 1957, not only have inactivated poliovirus vaccines come into widespread use but live attenuated vaccines have been submitted to intensive study and, in some countries, have been employed on a scale that could scarcely have been envisaged three years ago. These developments and the problems they raise are fully reviewed in the third report of the Expert Committee.

In most countries where inactivated vaccines have been widely used, the protection obtained has been of the order expected on the basis of controlled field trials. Manufacturing and testing problems appear to have diminished with increasing experience, but recent attempts to manufacture polyvalent vaccines containing poliomyelitis antigen have raised some special problems. Experience with such multiple antigens is still too limited for their value to be assessed.

The safety of live poliomyelitis vaccines appears to have been satisfactorily demonstrated in a number of areas where they have been used on a large scale, and in all except two of these areas the incidence of poliomyelitis has fallen. It is still too soon, however, to evaluate the long-term effectiveness of live vaccines. Criteria for evaluating the safety and effectiveness of such vaccines are formulated in the report. In this connection, further research on virus markers and on the degree of viremia produced by different strains is urgently needed. The capacity of the various strains to spread to contacts in the community is also a matter needing investigation. The Committee proposed criteria for the selection of suitable strains and for grading the various strains of the three sets of vaccines in use. They also gave attention to the possible contamination of live poliovirus vaccines by simian viruses, and recommended the study of their pathogenicity and methods of differential inactivation.

The choice of inactivated or live virus vaccine for large-scale immunization programs will depend upon the epidemiological, social and economic circumstances of the country concerned. The Committee examined the advantages and disadvantages of the two types of vaccine from these aspects and suggested a number of considerations to be kept in mind by public health authorities when deciding which policy to adopt. Emphasis is laid on the importance of serological surveys and surveillance for the efficient conduct of immunization programs. Finally, attention is drawn to the increasing prevalence of other enterovirus infections (Coxsackie and ECHO viruses), which cause a wide range of clinical manifestations, sometimes resembling those of poliomyelitis. Continued research is needed in this field, especially to detect any increase in the severity of the clinical manifestations in special groups—for example, in newborn infants.

**SPEECH SCIENCE. Acoustics in Speech. Richard A. Hoops. 130 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $5.25.**

This book furnishes a basis in the physical sciences for the understanding of the production of the sounds of speech. A Junior College textbook, it explains in clear, simple terms the meaning of sound, vibration, frequency, amplitude, wave motion, nature and effects of resonance, and vocal frequency. It deals also with times and duration in sounds, intensity and loudness, and voice quality. It is printed in clear large type with many diagrams which aid in comprehension of the facts provided.

A final chapter on voice quality deals in a detailed manner with the placement of tongue, palate and lips during normal voice production.

An addendum to each chapter, called "study aids", will be of service to those readers wishing to pass examinations.

There is no new material in this book, but a great deal of diverse material has been brought together and will be of service to students beginning to study speech pathology.

**EINFUHRUNG IN DIE INNERE MEDIZIN (INTRODUCTION TO INTERNAL MEDICINE). Hans Julius Wolf, Göttingen. 7th ed. 751 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1960. $10.00.**

This book, now in its seventh edition, is intended to acquaint the beginner with the field of internal medicine without presenting the overwhelming complexity of a complete textbook.

A short paragraph on the normal physiology of each organ precedes the discussion of the pathological disorders, their etiology, diagnosis and management. Some chapters are well written. Others omit essential facts or fail to stress them sufficiently, while matters of less importance are dealt with at length. A number of therapeutic suggestions are obsolete or even contraindicated in the light of modern knowledge.

The idea is good, but the work falls somewhat short of its goal.

*(Continued on page 72)*

CONNAUGHT

# IMMUNE SERUM GLOBULIN (HUMAN)

The production of Immune Serum Globulin (Human) by the Connaught Medical Research Laboratories has been made possible by the cooperation of the Canadian Red Cross Society, the Federal Government and the Governments of each of the Provinces.

Immune Serum Globulin is distributed by Provincial Departments of Health and also by the Canadian Red Cross Society through its regional blood depots for therapeutic purposes only. In addition, Immune Serum Globulin (Human) prepared from blood collected privately is available directly from the Laboratories on a regular sale basis.

Some of the conditions for which Immune Serum Globulin is indicated are:

| | |
|---|---|
| **Measles (rubeola)** | —For prevention and modification. |
| **Hypogammaglobulinæmia and Agammaglobulinæmia** | —For maintenance of the patient's resistance to infection. |
| **Infectious Hepatitis** | —For close contacts or in the control of outbreaks. |
| **Poliomyelitis** | —For prevention and modification. |
| **German Measles (rubella)** | —For prevention during early pregnancy. |

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Canad. M. A. J.
Jan. 7, 1961, vol. 84

*(Continued from page 70)*

**LOCAL HEALTH SERVICE. Third Report of the Expert Committee on Public Health Administration. World Health Organization, Geneva, Switzerland, 1960. 60 cents.**

In this report a good description is given of methods for local health surveys. These surveys cover not only traditional local health services, but also general social and economic conditions, occupational health, general practice, hospital and other institutional services, veterinary service, and rehabilitation. In Canada, the report will be useful to all those concerned with the planning of health services, at the local, provincial and federal levels, including medical associations and practising physicians.

As an appendix to the report a brief description is given of pilot local health studies carried out in selected areas in India, The Netherlands, Puerto Rico, Sweden and the Union of South Africa.

**ADVENTURE TO MOTHERHOOD. The Picture Story of Pregnancy and Childbirth. J. Allan Offen. 72 pp. Illust. Audio Visual Education Company of America, Taplinger Publishing Co., Inc., New York, 1960. $2.95.**

"Adventure to Motherhood" purports to "tell a story which is nearly as old as time itself", according to the preface by the author. The story, which is in effect one man's handling of a nice middle-class private practice, is told in coloured pictures with a short text. The old part of the story is told by reproduction of some of the excellent Maternity Centre Association's diagrams which, unfortunately, have suffered in the colour process.

As this small book is designed to help prospective parents understand what is ahead of them in pregnancy, it was loaned to several patients for their comments. Most of them thought that they learned little, and many were rather hurt to find that the mother-to-be seemed to have little say in what was happening to her. The general feeling of dissatisfaction was summed up by one woman who commented that "The Canadian Mother and Child" at 35 cents' maximum cost was a much better buy.

**DIABETES MELLITUS. A Clinical and Pathological Study of 2529 Cases. E. T. Bell. 63 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $4.00.**

Characteristic of the American Lecture Series, this little monograph of 65 pages, including several good illustrations, tells a story beautifully. Dr. Bell, Emeritus Professor of Pathology at the University of Minnesota, is a world-renowned pathologist who has made a particular study of renal disease and diabetes. The approach is clinical and physiological but the large amount of original pathological data that he provides, prevents idle speculation. The present position and the limitations of our knowledge of diabetes are clearly delineated. The complications, particularly the vascular ones, are thoroughly dealt with. The eye lesions are not.

Ogilvie* would not agree with his statement that normal beta cells are present in appreciable numbers of adult diabetics, but Bell did not use Ogilvie's laborious procedure of counting beta cells. No electron microscope work is included. It is a pity that such a beautifully produced monograph should have the gross errors in proof-reading that occur on page 3 and pages 12 and 13.

This book is a gem of clear thinking that would delight any student of medicine interested in the basic understanding of diabetes.

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*MACLEAN, N. AND OGILVIE, R. F.: *Diabetes*, 4: 367, 1955.

## ASSOCIATION NOTES

*(Continued from page 55)*

Council will be held as usual on Tuesday evening. Golfing enthusiasts will also have an opportunity of competing for the annual trophy.

There will be a special ladies' program for doctors' wives, and the centre of activity will be the hospitality room where ladies will meet and plan their day's activities. As well as joining their husbands in the general social program, ladies will lunch at the Montreal Museum for Fine Arts on Wednesday, June 21; and on the following day, Canadian-born Mrs. William Mackersie, president of the Women's Auxiliary of the American Medical Association, will address a luncheon meeting. Plenty of local sightseeing and shopping excursions will be available to make the ladies' stay in Montreal a memorable occasion.

Additional details and adjuncts to the scientific and social programs will be published in the Journal as the time of the meeting approaches.

### A Word About Montreal

Montreal is Canada's largest and greatest tourist city, and its unique charm and atmosphere, its friendliness, hospitality and the courtesy of its citizens, have accounted for its tremendous popularity with visitors from Canada and abroad. Of interest to the visitor is the fact that Montreal is an island which is 30 miles long, between 7 and 10 miles wide, and has an area of 194 square miles. The city proper occupies about half of the island, being 50 square miles in area. It is the second largest French-speaking community in the world, being second only to Paris, France. While three-quarters of the population are of French Canadian origin, and the balance, mainly of Anglo-Saxon and other origins, the city is almost totally bilingual.

Montreal's leading hotels are the Queen Elizabeth, the Sheraton Mount Royal, the Laurentien, the Windsor, the Queen's, the Hotel de la Salle, the Berkeley, the Ritz Carlton, the Royal Embassy, and the New Carlton Hotel. All of these hotels feature fine food in their dining rooms, and luxurious and comfortable appointments.

More news about our host city will appear in subsequent issues of the Journal.

# MEDICAL NEWS *in brief*

*(Continued from page 54)*

## THE EARLY RADIOLOGICAL SIGNS OF RHEUMATOID ARTHRITIS

The most important of the radiological signs of rheumatoid arthritis, for diagnostic purposes, are the early ones. Based on a prolonged serial study of patients, starting in 1940, at the Postgraduate Medical School of London, a description of these changes has been reported by Waters (*Bull. Rheumat. Dis.*, 11: 231, 1960).

(1) Soft tissue changes: While an increase in soft tissue shadows due to effusion is probably the very earliest sign of rheumatoid arthritis, this is best appreciated clinically.

(2) Bone rarefaction: In a similar way, rarefaction of bone, due to decreased use caused by pain, is a useful localizing sign when comparing bilaterally symmetrical regions. The character of bone rarefaction may give information on the duration of disuse; it is paraepiphyseal or often spotty in acute disuse, more widespread and involving shaft cortices in prolonged disuse, and coarsely trabeculated in cases of intermittent involvement.

(3) Periosteal elevation and ossification: The third type of change to develop, in temporal terms, is periosteal elevation and ossification. Like the two preceding changes, this frequently antedates erosion, although it may also be seen with it. It is due to an inflammatory (i.e. high protein content) edema affecting that part of the periosteum in contiguity with the inflamed joint and, unlike rarefaction, it is confined to the bones comprising that joint. It is always more pronounced and thicker nearest the joint and may become lamellated. Ultimately the new subperiosteal bone fuses with cortical bone and then becomes undetectable except by comparison with earlier films or with a contralateral unaffected joint, appearing merely as a thickened neck. Finally the new bone may be entirely resorbed. This type of lesion must be differentiated from new subperiosteal bone produced in normal rapid growth, and from the slower changes of adaptive remodelling often seen in feet, particularly where disease, fracture or operation imposes a new posture.

*(Continued on page 36)*

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along the continuum from mild anxiety to severe psychosis.

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| hospitalized psychotics | 100 mg. t.i.d. | (200-800 mg.) |
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SUPPLIED: Mellaril tablets, 10 mg., 25 mg., 100 mg.

SANDOZ PHARMACEUTICALS SANDOZ DORVAL, P.Q.

MEDICAL NEWS *in brief*

*(Continued from page 35)*

(4) Erosions: The most definitive radiological change is the erosion, which may be a surface or a pocketed defect (pseudocyst). It implies removal of bone substance and is nearly always irreversible.

(5) Narrowed joint space: The fifth type of change is narrowing of the joint space. This implies loss of articular cartilage in the appositional area and is seldom seen as a presenting sign in the metacarpophalangeal joints. It is, however, quite often seen as the first sign in interphalangeal joints, and in the wrist, carpus, tarsus, knee and hip.

(6) Radiographic changes in juvenile rheumatoid arthritis: Radiological evidence of joint inflammation in the young may exist without narrowing, cysts, erosion, periostitis or soft tissue swelling. In early childhood premature appearance of epiphyseal centres, increased or sometimes decreased longitudinal growth and general increase in size of both epiphysis and diaphysis may be seen. In later childhood, premature fusion of the epiphyseal line occurs in affected joints, leading to cessation or distortion of bone growth. Measurement of the distances between lines of arrested growth will frequently demonstrate a unilateral growth abnormality and give some idea of the time of its occurrence.

None of the above changes by itself is specific for rheumatoid arthritis. In the early stages, however, when the disease is often intermittent or "palindromic", such a radiological change may provide an essential clue to the correct diagnosis, even in the absence of contemporary clinical residua.

---

## "Are the xanthines effective in ANGINA PECTORIS?"

(Abstract of the paper with above title)

A favorable response was unequivocally demonstrated with aminophylline when administered intravenously to angina pectoris patients. In sharp contrast the author, noted for his original contributions to cardiovascular research, found oral administration ineffective in all patients tested. This suggested that the failure was correlated with subthreshold theophylline blood-levels obtained with oral administration.

A 20% alcohol-solution of theophylline (Elixophyllin®) has been shown to provide blood levels comparable to those obtained with I.V. administration of aminophylline. This oral preparation and a placebo (identical in appearance, taste and alcoholic content) were tested by the electrocardiographic response obtained and by a double-blind clinical evaluation.

The author reported: "In the light of these findings, conclusions derived from animal experiments which have classed theophylline as a 'malignant' coronary vasodilator must be rejected for man." Elixophyllin administered orally to 30 patients was effective "not only in control of symptoms but in its modifying action on the electrocardiographic response to standard exercise. The efficacy of this preparation is based on the rapid absorption and attainment of high blood levels made possible by the vehicle employed."

(Russek, H. I., Am. J. Med. Sc. Feb., 1960)

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**ORAL DOSAGE:** First 2 days—doses of 45 cc. t.i.d. (before breakfast, at 3 P.M., and on retiring).
Thereafter—doses of 30 cc. t.i.d. (at same times).

**AVAILABLE:** Prescription only; bottles of 16 fl. oz. and 1 gallon.

**SPECIAL REPRINT:** Reprint of Dr. Russek's paper abstracted above on request.

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## PHOTOSCANNING IN DIAGNOSIS OF CARDIAC ENLARGEMENT

Use of photoscanning to differentiate cardiac enlargement from pericardial effusion in a series of 50 patients was reported to the American Heart Association in St. Louis, by Dr. Henry N. Wagner Jr. and associates of Johns Hopkins Hospital, Baltimore. The radioactivity image recorded by the photoscanner is superimposed on the roentgenogram of the heart, and the two images are brought into register through common localizing markers. To avoid magnification of the cardiac silhouette by the divergent x-ray beam, the background chest film is made in two sections. The scanning image is recorded after 100 $\mu$c. of $I^{131}$-labelled human serum albumin has been injected intravenously and permitted to diffuse for at least five minutes.

With cardiac dilatation and/or hypertrophy, borders of the cardiac blood pool as picked up by the photoscan correspond with those of the enlarged cardiac silhouette on the x-ray. With pericardial effusion, the transverse diameter of the x-ray image is greater than that of the cardiac blood pool on the scan. In 13 patients subsequently proved to have effusion, the ratio of the maximum diameter on the scan to the maximum x-ray diameter was 57% (plus or minus 12%), while the ratio with cardiac enlargement was 95% (plus or minus 8%).

Clinically, the technique has proved most useful for ruling out pericardial effusion in patients with heart failure of obscure etiology. In no instance was pericardial infusion present when the procedure indicated cardiac dilatation. In three instances, the method indicated a diagnosis of effusion which was not borne out by paracentesis. One of these false positives was in a patient who showed a marked discrepancy between cardiac blood pool and x-ray silhouette. Operation revealed a huge lipoma practically surrounding the heart but confined within the pericardial sac. —*Medical News*, November 9, 1960.

—

## RISTOCETIN AND TUBERCULOSIS

In the November 1960 issue of *The American Review of Respiratory Diseases*, Drs. Helen Holden of the Nova Scotia Sanatorium, S. J. Shane of the Halifax Health Centre and C. E. van Rooyen of the Department of Bacteriology, Dalhousie University, report the results of a small-scale study carried out by the Tuberculosis Division of the Halifax Health Centre and the Nova Scotia Sanatorium with the purpose of investigating the therapeutic efficacy of the recently developed broad-spectrum antibiotic, ristocetin, in the treatment of tuberculosis.

From observations of the effects of this drug on 11 patients, it was concluded that ristocetin is of no value in the treatment of tuberculosis and that even in low daily doses it would be too toxic to justify long-term administration.

—

## SIMPLIFIED PROTHROMBIN TEST

Satisfactory results with the Manchester simplified prothrombin time determination test with 100 patients receiving anticoagulant therapy over a 10-month period were reported by Dr. William T. Foley, Associate Professor of Medicine at Cornell University Medical College, to the Beth Israel Hospital monthly cardiovascular conference. With the Manchester test, results were achieved that compared favourably with those obtained by more complicated tests. The test may prove useful in physicians' offices for the maintenance and management of patients on anticoagulant therapy. In the procedure, blood is obtained from the fingertip instead of intravenously; the glass slide is maintained at a constant temperature of 37°C. by means of an electric heating device with a built-in stop watch. The findings are available within two or three minutes, and the physician can then prescribe the proper anticoagulant dosage. — *Medical Tribune*, November 14, 1960.

## EUROPEAN SYMPOSIUM ON GONORRHEA AND NON-GONOCOCCAL GENITOURINARY INFECTIONS

A symposium on gonorrhea and non-gonococcal genitourinary infections, organized by the Polish Dermatological Society and the European Office of the International Union against the Venereal Diseases and the Treponematoses

*(Continued on page 40)*

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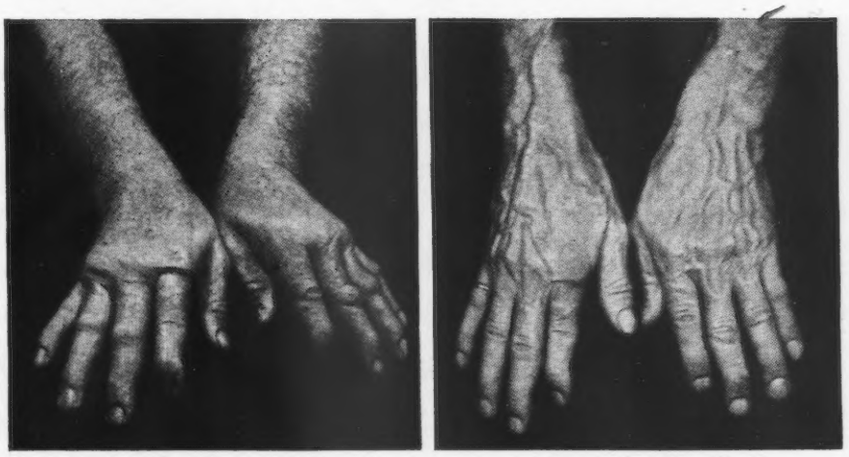

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1330

MEDICAL NEWS *in brief*

*(Continued from page 37)*

(IUVDT) was held in Krakow, Poland, September 26 to October 1, 1960. Experts from Denmark, Finland, France, Germany, Italy, Poland, Portugal, Tunisia, the United Kingdom and the United States of America, and from the World Health Organization participated in the program.

The report of this symposium contains important considerations and recommendations, particularly relating to the failure of gonorrhea control in most countries, the absence of an international method for determining penicillin sensitivity of the gonococcus and the dosage and type of penicillin preparations now required. The participants expressed general agreement with the following observations and recommendations.

The overall incidence of gonorrhea has increased in many countries in recent years. It is among the most frequently reported diseases in some areas in Europe and in other regions. The increase in incidence is particularly marked in the younger age groups and there remains a large undiagnosed reservoir in women. There is evidence that serious complications and sterility in the female are much more common as a consequence of this disease than was believed to be the case in the earlier years of antibiotic therapy. Vulvovaginitis in infants continues to be encountered in some countries and ophthalmia neonatorum has not been eliminated as a hazard of the newborn.

It is recognized that in spite of the early individual successes in the treatment of gonorrhea with penicillin and the subsequent wide availability and use of this antibiotic over 15 years, it has not been possible to control the disease in the mass of patients. The reasons for this failure relate on the one hand to the nature of the infection, its mode of spread and epidemiological characteristics as well as to the shortcomings of the techniques for defining and localizing the reservoir of infection and diagnosing the disease, particularly in the female; and, on the other hand, to the increasing difficulties experienced in the management of the disease, including its treatment with antibiotics.

Clinical resistance to penicillin treatment is now being observed increasingly in many countries and to streptomycin in some countries. This development may continue. Microbiological evidence suggests a gradual development in the laboratory of penicillin resistance of *N. gonorrhoeae*, and in some instances a more abrupt development of resistance to streptomycin. It will be extremely important to the profession and health administrations in all countries to follow this problem closely in the future. However, laboratory methods for the determination of the susceptibility of *N. gonorrhoeae* to antibiotics, particularly to penicillin, do not permit meaningful comparisons within or between countries at the present time. The establishment of international standard methods in this respect is, therefore, urgent.

Penicillin remains the drug of choice in the treatment of gonorrhea in both sexes. Penicillin reactions occur, but their incidence is not alarming. However, all precautions should be taken and suitable measures should be available

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in case of acute anaphylactic reactions. Penicillin dosages used in the treatment of gonorrhea should be increased to as much as 1.8 million units in the male. A suitable mixture of fast-acting penicillin, such as procaine penicillin G, and prolonged-acting penicillin, such as benzathine penicillin, should be used to destroy *in situ* all gonococci, including those with the lowest known sensitivity, and to provide sufficiently long exposure (at least 48 hours) of locally phagocytosed live gonococci to prevent relapse. Microbiological selection as well as possible mutagenic effects which may result in the future from long-acting penicillin are, on present evidence, probably of secondary importance in considering the immediate problems now confronting gonorrhea control.

There is a need for development of a simple rapid serological test for early diagnosis and specific detection of the gonococcus, particularly in the female. Recent research advances in defining the antigen fractions of the gonococcus, particularly the capsular elements, do not preclude such a development in spite of previous concepts of the immunology of gonococcal infections. These concepts may also allow for new approaches to the ultimate possibility of developing an immunizing agent against gonococcal infection.

Further exchange of scientific information on the epidemiological, clinical and control aspects of gonorrhea is needed between members of the medical profession and health administrations throughout the world in order to maintain awareness of the changing aspects of the gonorrhea problem.

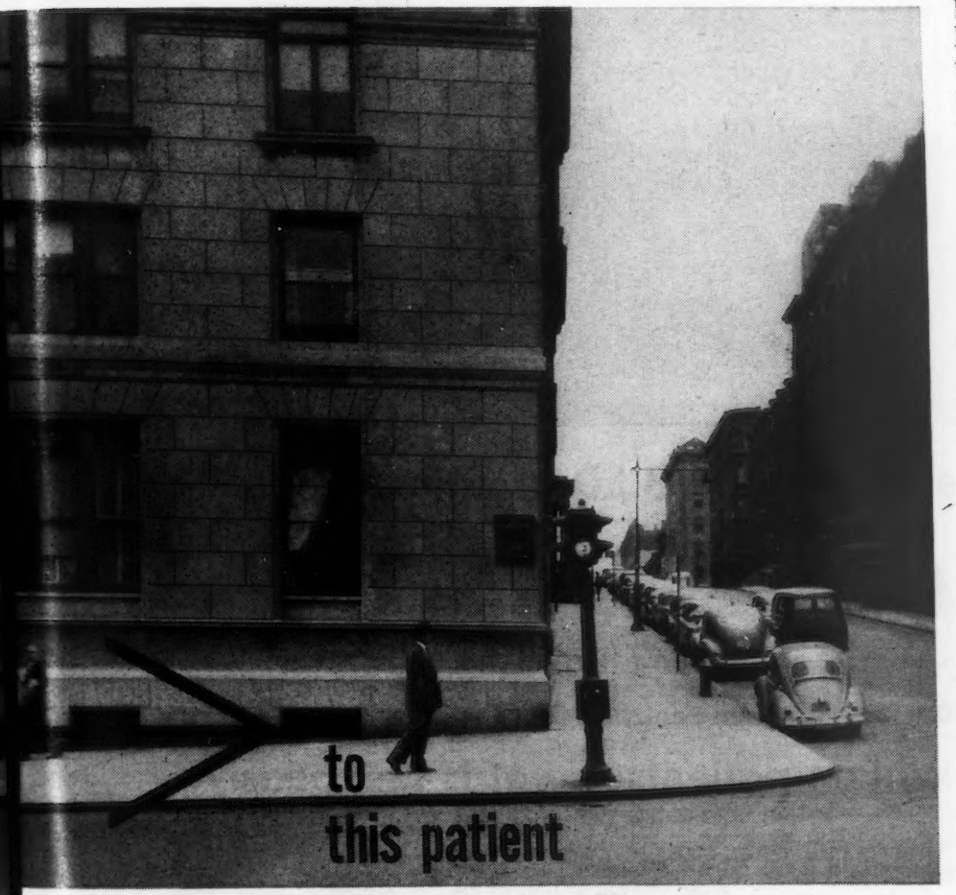
—

## EPIDEMIOLOGY OF URINARY TRACT INFECTIONS

A survey of urinary tract infections was conducted in 3057 school children in a small city located in th Shenandoah Valley of Virginia, by methods which permitted rapid detection of significant bacteriuria in a large non-hospital population. A colony count of 100,000 or greater per ml. of urine was found to be the most useful criterion of infection in urine specimens obtained under "field" conditions. Comparison of clean-voided urine specimens collected under "field" conditions from girls versus catheterized specimens from the same subjects revealed that all children with urine containing fewer than 100,000 organisms per ml. had counts of less than 1000 on catheterization, whereas 43% of children whose urine contained more than 100,000 organisms per ml. had similar high counts on catheterization.

Kunin, Southall and Paquin (*New England J. Med.*, 263: 817, 1960) found 15 girls with significant bacteriuria, all but one of whom had common urinary pathogens. No infections were encountered in the 1647 boys. The overall prevalence of urinary tract infection in the surveyed group of girls was 1%. This rate is the minimal incidence, since at least five other girls not included were under treatment for urinary tract infections during the study period in this community. (Eighty-five per cent of the children enrolled in the city schools participated in the study.)

*(Continued on page 43)*

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With "Falapen", it is unnecessary to administer penicillin every six to eight hours for full effectiveness. Studies have shown that one "Falapen" tablet every 12 hours has controlled scarlet fever, otitis media, pharyngitis and pneumococcal and gonococcal infections.

"FALAPEN" is relatively safe; when compared with parenteral administration of penicillin, oral administration is associated with much lower incidence of severe sensitivity reactions.

**DOSAGE:** Adults: One tablet every 12 hours. This may be increased for very severe infections.
*Bottles of 10 tablets.*

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Newly-developed "Polymer 37"* coating resists stomach acid action but dissolves immediately in the intestine, exposing the penicillin core.

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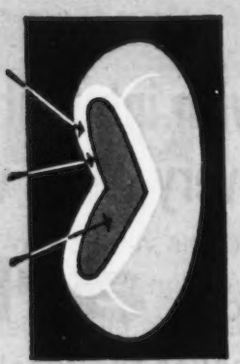

*Pat. 1959

**CAUTION:** In rare instances, the injection of penicillin, and more rarely still its oral administration, may cause acute anaphylaxis. The reaction appears to occur more frequently in patients with bronchial asthma and other allergies, or in those who have previously demonstrated sensitivity to penicillin.

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MEDICAL NEWS *in brief*

*(Continued from page 41)*

Eighty per cent of the organisms isolated from the urine of the suspect girls were *E. coli*, three strains of which were resistant to 50μg. of tetracycline per ml. Intravenous pyelograms in the 15 girls revealed reduplication of the pelvis in two, a ptotic kidney in one and hydronephrosis and hydroureter in another. Cystograms in 13 of the girls showed marked vesicoureteral reflux in two, suggestive reflux in two and a trabeculated bladder suggestive of bladder neck obstruction in one. Corollary studies revealed transient proteinuria in 2.8% of the children. Only four of the 3057 children had significant glycosuria (0.13%); two were known to have diabetes.

—

## NEW BLOOD DILUTION PIPETTE

A simple and accurate blood dilution pipette that eliminates human error associated with blood collection, measurement, and dilution has been developed in Linden, New Jersey, by researchers of the Esso Research and Engineering Company. The disposable, self-filling, self-measuring unit consists of a straight, thin-bore glass capillary and detachable plastic reservoir containing a premeasured volume of diluent. By capillary action blood is drawn into the tube immediately on contact with the tip of the capillary, and stops when the liquid has reached the end of the capillary. The possibility of error on the part of the laboratory assistant is therefore eliminated, since the technician does not have to draw the blood up to a scribe mark on the pipette.

The erythrocyte and leukocyte counts have been checked electronically for accuracy and have been found to be comparable with those obtained with current high-quality glass dilution blood pipettes. — *Medical Tribune*, November 7, 1960.

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## CANADIAN RED CROSS SENDS ADDITIONAL MEDICAL TEAM TO CONGO REPUBLIC

Four Canadian doctors have accepted Red Cross assignments to the medical teams serving in the Congo Republic. They are Dr. Edmund V. Currie, Valois, Quebec; Dr. Robert Timmons and Dr. Richard T. Wilson of Montreal; and Dr. G. E. Stoker of Toronto. D. Bruce Shaw, chairman of the national executive of the Canadian Red Cross, said that the Society will maintain a team of five doctors in the Congo for at least three months longer. This decision was based on a policy established at the recent meeting of the Executive Committee of the League of Red Cross Societies in Geneva, which Mr. Shaw attended. At the meeting, the United Nations, through the World Health Organization, urged the League of Red Cross Societies and its 85 members, the national Red Cross and Red Crescent Societies of the world, to continue medical participation in the Congo Republic during the emergency situation. Mr. Shaw stated that the 20 national Red Cross Societies which now have teams in the Congo agreed to the decision at the Red Cross meetings.

Dr. Wilson, who heads the Canadian Red Cross team, was engaged in private practice in Montreal before his appointment, specializing in internal medicine. He is a staff physican at St. Mary's Hospital and is in charge of the hospital's chest clinic. Dr. Currie is a native of Saskatchewan. He has been given leave of absence from his position as senior medical officer of the Northern Electric Company. Dr. Timmons is a native of Quebec. For the past three years he has been a surgeon at l'Hôpital Ste-Jeanne d'Arc in Montreal. Dr. Stoker is medical director of the Toronto Depot of the Canadian Red Cross blood transfusion service. He is stationed in Leopoldville and is in charge of the emergency blood transfusion service established there in July by the International Red Cross. All four doctors are bilingual in English and French. The fifth member of the Canadian Red Cross medical team is an anesthetist, Dr. Raymond Allard of Montreal, who arrived in the Congo in the middle of September. Dr. Jonathan Sinclair, Toronto, and Dr. Philip Edwards, Dorion, who have been serving as Canadian Red Cross medical representatives in the Congo Republic since last July, returned to Canada in November.

Long-acting oral penicillin makes bed rest more effective, too

An old saw wisely says there is only one thing all people like that is good for them: a good night's sleep. True enough — but even truer for the sick *who need sleep* most. Consider the patient on oral penicillin who is wakened from sound slumber for additional medication. Sleep is interrupted, and, what is worse, getting back to sleep is often difficult.

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1. Malkin, S.: Canad. M.A.J. 81:553, 1959. 2. Grignon, C.-E., and Leboeuf, B.: L'Union Médicale du Canada 87:1198, 1959. 3. Hébert, A.: Canad. M.A.J. 80:293, 1959. 4. Rocha, H., Chalem, F. and Pena, M.A.: Revista de la Facultad de Medicina, Universidad Nacional, Bogota, Colombia 27:145, 1959.

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